



human subject diagnosed with cystic fibrosis, comprising administering to the subject, in a pharmaceutically acceptable carrier, an effective amount of a fusion protein, comprising a cystic fibrosis transmembrane conductance regulator (CFTR) and a membrane translocation sequence (MST), whereby the fusion protein can be taken up by affected cells in the subject, thereby treating cystic fibrosis. The present invention also provides a fusion protein comprising a cystic fibrosis transmembrane conductance regulator and a membrane translocation sequence.

L2 ANSWER 3 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1  
AN 2004:814996 CAPLUS  
DN 141:348634  
TI The Host Resistance Locus sst1 Controls Innate Immunity to Listeria monocytogenes Infection in Immunodeficient Mice  
AU Boyartchuk, Victor; \*\*\*Rojas, Mauricio\*\*\* ; Yan, Bo-Shiun; Jobe, Ousman; Hurt, Nicholas; Dorfman, David M.; Higgins, Darren E.; Dietrich, William F.; Kramnik, Igor  
CS Program in Gene Function and Expression, University of Massachusetts Medical School, Boston, MA, 02115, USA  
SO Journal of Immunology (2004), 173(8), 5112-5120  
CODEN: JOIMA3; ISSN: 0022-1767  
PB American Association of Immunologists  
DT Journal  
LA English  
AB Epidemiol., clin., and exptl. approaches have convincingly demonstrated that host resistance to infection with intracellular pathogens is significantly influenced by genetic polymorphisms. Using a mouse model of infection with virulent *Mycobacterium tuberculosis* (MTB), we have previously identified the sst1 locus as a genetic determinant of host resistance to tuberculosis. In this study we demonstrate that susceptibility to another intracellular pathogen, *Listeria monocytogenes*, is also influenced by the sst1 locus. The contribution of sst1 to anti-listerial immunity is much greater in immunodeficient scid mice, indicating that this locus controls innate immunity and becomes particularly important when adaptive immunity is significantly depressed. Similar to our previous observations using infection with MTB, the resistant allele of sst1 prevents formation of necrotic infectious lesions in vivo. We have shown that macrophages obtained from sst1-resistant congenic mice possess superior ability to kill *L. monocytogenes* in vitro. The bactericidal effect of sst1 is dependent on IFN- $\gamma$  activation and reactive oxygen radical prodn. by activated macrophages after infection, but is independent of NO prodn. It is possible that there is a single gene that controls common IFN-dependent macrophage function, which is important in the pathogenesis of infections caused by both MTB and *L. monocytogenes*. However, host resistance to the two pathogens may be controlled by two different polymorphic genes encoded within the sst1 locus. The polymorphic gene(s) encoded within the sst1 locus that controls macrophage interactions with the two intracellular pathogens remains to be elucidated.  
RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 31 MEDLINE on STN  
AN 2004244582 MEDLINE  
DN PubMed ID: 15143481  
TI Differential induction of apoptosis and necrosis in monocytes from patients with tuberculosis and healthy control subjects.  
AU Gil Diana P; Leon Laura G; Correa Lucia I; Maya Jose R; Paris Sara C; Garcia Luis F; \*\*\*Rojas Mauricio\*\*\*  
CS Grupo de Inmunologia Celular e Inmunogenetica, Facultad de Medicina, Universidad de Antioquia, Medellin, Colombia.  
SO Journal of infectious diseases, (2004 Jun 1) 189 (11) 2120-8.  
Journal code: 0413675. ISSN: 0022-1899.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Abridged Index Medicus Journals; Priority Journals  
EM 200407  
ED Entered STN: 20040515  
Last Updated on STN: 20040723

Entered Medline: 20040722

AB BACKGROUND: *Mycobacterium tuberculosis* and purified protein derivative (PPD) induce apoptosis in murine macrophages and apoptosis and necrosis in human monocytes and alveolar epithelial cells. Macrophages from bronchoalveolar lavages and granulomas from patients with tuberculosis (TB) present both types of cell death; however, the significance of the type of cell death in TB remains uncertain. METHODS: Monocytes from PPD-positive control subjects and from patients with TB were exposed to PPD or *M. tuberculosis*. Apoptosis, necrosis, and the percentage of tumor necrosis factor (TNF)-alpha-positive and interleukin (IL)-10-positive cells were determined cytofluorometrically. Levels of lactate dehydrogenase, TNF-alpha, and IL-10 were measured in culture supernatants. The role of TNF-alpha and IL-10 was tested by blockade experiments. RESULTS: PPD and *M. tuberculosis* induced apoptosis in monocytes from PPD-positive control subjects, whereas cells from patients with TB presented apoptosis and necrosis. Cells from PPD-positive control subjects produced mainly TNF-alpha, whereas cells from patients with TB produced mainly IL-10. Blockade experiments suggest that TNF-alpha and IL-10 regulate the type of cell death occurring in response to *M. tuberculosis*. CONCLUSIONS: Results suggest that apoptosis of monocytes exposed to mycobacteria may partly explain the protective immune response found in PPD-positive control subjects, whereas necrosis may be determinant of the bacterial dissemination and tissue damage that occur in patients with active TB.

L2 ANSWER 5 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2  
AN 2003:603564 CAPLUS  
DN 139:336786  
TI Structure and Function of CD72 in the Non-obese Diabetic (NOD) Mouse  
AU Rojas, Andres; Xu, Fingping; \*\*\*Rojas, Mauricio\*\*\* ; Thomas, James W.  
CS Departments of Medicine, Microbiology and Immunology, Vanderbilt  
University Medical Center, Nashville, TN, 37232-2681, USA  
SO Autoimmunity (2003), 36(4), 233-239  
CODEN: AUIMEI; ISSN: 0891-6934  
PB Taylor & Francis Ltd.  
DT Journal  
LA English  
AB Type I or insulin dependent diabetes mellitus develops in the non-obese diabetic (NOD) mouse as a consequence of T cell mediated autoimmune attack on pancreatic beta cells. B lymphocytes are required for disease progression in NOD and loss of tolerance in the B cell compartment is one of the earliest manifestation of the autoimmune process. To understand how the fate and function of B lymphocytes may be regulated in the context of an organ specific autoimmune disease, the B cell co-receptor CD72 (Lyb-2) was examined in NOD mice. Mab that recognize a, b, and d alleles of CD72 reacted poorly with NOD B cells while western blots of B cell extracts show that CD72 is abundant in NOD B cells. Nucleotide sequencing of CD72 cDNA confirms that an uncommon allele, CD72c, is expressed in NOD. Functional studies using monoclonal antibodies indicate that the CD72c allele of NOD can serve as a pos. regulator of B cell responses both as a single signal and in synergy with BCR or IL-4 stimulation. Since CD72c differs principally in the extra cellular or ligand binding portion of the mol., interactions with its natural ligand in vivo may contribute to functional differences in mouse strains that express this allele. NOD and lupus prone strains share the CD72c allele and its functions may contribute to overlapping features of organ specific and systemic autoimmune disorders.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3  
AN 2003:564026 CAPLUS  
DN 139:390755  
TI Modulation of macrophage apoptosis by antimycobacterial therapy: physiological role of apoptosis in the control of *Mycobacterium tuberculosis*  
AU Gil, Diana; Garcia, Luis F.; \*\*\*Rojas, Mauricio\*\*\*  
CS Facultad de Medicina, Grupo de Inmunología Celular e Inmunogenética, Universidad de Antioquia, Medellin, Colombia  
SO Toxicology and Applied Pharmacology (2003), 190(2), 111-119  
CODEN: TXAPA9; ISSN: 0041-008X

PB Elsevier Science  
DT Journal  
LA English  
AB Apoptosis is a form of cell death that avoids inflammatory responses. We had previously reported that *Mycobacterium tuberculosis* (Mtb) and Purified Protein Deriv. (PPD) induce apoptosis in murine macrophages. The prodn. of TNF. $\alpha$ . and IL-10 in response to Mtb infection modulates apoptosis by controlling nitric oxide prodn. and caspase activation. Furthermore, Mtb triggers calcium influx responsible for mitochondrial alterations, an early pathway of apoptosis, independently of TNF. $\alpha$ . and IL-10. In tuberculosis patients apoptotic macrophages are found in granulomas and bronchoalveolar lavages, suggesting that apoptosis may participate in the control of Mtb. To further explore the role of macrophage apoptosis in tuberculosis, we studied the capacity of std. antimycobacterial drugs to modulate different events assocd. with the induction of apoptosis. The B10R murine macrophage line was infected or not with Mtb (5:1 bacteria to macrophage ratio) or exposed to PPD (10  $\mu$ g/mL), in the presence or absence of varying concns. (1-20  $\mu$ g/mL) of anti mycobacterial drugs (isoniazid, rifampin, thiacetazone, streptomycin, and ethambutol). Inhibition of the intracellular growth of *M. tuberculosis* by all drugs studied/correlated with inhibition of permeability transition (PT) alterations; TNF. $\alpha$ ., IL-10, and nitric oxide prodn., and caspase-1 activation. However, these drugs did not affect PPD-induced apoptosis or its assocd. events, suggesting that the ability of antimycobacterial drugs to block macrophage apoptosis could be explained by their effects on the metabolic activities of Mtb. All drugs, except isoniazid, at higher concns., induced PT alterations in noninfected macrophages in a way that appears to be dependent on calcium, since a calcium chelator prevented it. The results presented herein suggest that the pharmacol. manipulation of pathways assocd. with macrophage apoptosis may affect the intracellular growth of Mtb.

RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 7 OF 31 USPATFULL on STN  
AN 2002:259566 USPATFULL  
TI Sequence and method for genetic engineering of proteins with cell membrane translocating activity  
IN Lin, Yao-Zhong, Nashville, TN, UNITED STATES  
Donahue, John P., Nashville, TN, UNITED STATES  
\*\*\*Rojas, Mauricio\*\*\* , Nashville, TN, UNITED STATES  
Tan, ZhongJia, Nashville, TN, UNITED STATES  
PA Vanderbilt University (U.S. corporation)  
PI US 2002143142 A1 20021003  
US 6780843 B2 20040824  
AI US 2002-116288 A1 20020404 (10)  
RLI Division of Ser. No. US 2000-562868, filed on 1 May 2000, PENDING  
Division of Ser. No. US 1998-186170, filed on 4 Nov 1998, GRANTED, Pat. No. US 6248558

PRAI US 1998-80083P 19980331 (60)

DT Utility

FS APPLICATION

LREP NEEDLE & ROSENBERG P C, 127 PEACHTREE STREET N E, ATLANTA, GA, 30303-1811

CLMN Number of Claims: 73

ECL Exemplary Claim: 1

DRWN 9 Drawing Page(s)

LN.CNT 1586

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention describes a membrane-translocating peptide sequence (MTS) which facilitates entry of polypeptides and proteins into cells. Also described is an isolated nucleotide sequence encoding the membrane-translocating peptide and a method of using this sequence to genetically engineer proteins with cell membrane permeability. The MTS, and the method of genetically engineering proteins with cell membrane permeability, are useful for polypeptide and protein delivery for human and veterinary applications such as vaccine delivery and cancer therapy.

L2 ANSWER 8 OF 31 USPATFULL on STN

AN 2002:201877 USPATFULL

TI Sequence and method for genetic engineering of proteins with cell

IN membrane translocating activity  
Lin, Yao-Zhong, Nashville, TN, United States  
Donahue, John P., Nashville, TN, United States  
\*\*\*Rojas, Mauricio\*\*\*, Nashville, TN, United States  
Tan, ZhongJia, Nashville, TN, United States  
PA Vanderbilt University, Nashville, TN, United States (U.S. corporation)  
PI US 6432680 B1 20020813  
AI US 2000-562868 20000501 (9)  
RLI Division of Ser. No. US 1998-186170, filed on 4 Nov 1998, now patented,  
Pat. No. US 6248558  
PRAI US 1998-80083P 19980331 (60)  
DT Utility  
FS GRANTED  
EXNAM Primary Examiner: Low, Christopher S. F.; Assistant Examiner: Kam,  
Chih-Min  
LREP Needle & Rosenberg, P.C.  
CLMN Number of Claims: 12  
ECL Exemplary Claim: 1  
DRWN 15 Drawing Figure(s); 9 Drawing Page(s)  
LN.CNT 1419  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB The invention describes a membrane-translocating peptide sequence (MTS)  
which facilitates entry of polypeptides and proteins into cells. Also  
described is an isolated nucleotide sequence encoding the  
membrane-translocating peptide and a method of using this sequence to  
genetically engineer proteins with cell membrane permeability. The MTS,  
and the method of genetically engineering proteins with cell membrane  
permeability, are useful for polypeptide and protein delivery for human  
and veterinary applications such as vaccine delivery and cancer therapy.

L2 ANSWER 9 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4  
AN 2002:512290 CAPLUS  
DN 138:37469  
TI Mycobacterial lipoarabinomannans: modulators of dendritic cell function  
and the apoptotic response  
AU Nigou, Jerome; Gilleron, Martine; \*\*\*Rojas, Mauricio\*\*\* ; Garcia, Luis  
F.; Thurnher, Martin; Puzo, Germain  
CS Institut de Pharmacologie et de Biologie Structurale, CNRS, Toulouse,  
31077, Fr.  
SO Microbes and Infection (2002), 4(9), 945-953  
CODEN: MCINFS; ISSN: 1286-4579  
PB Editions Scientifiques et Medicales Elsevier  
DT Journal; General Review  
LA English  
AB A review. The mol. bases of Mycobacterium tuberculosis pathogenicity  
remain unclear. The authors report here how M. tuberculosis mannosylated  
lipoarabinomannans contribute to the survival of bacilli in the human  
reservoir by (i) inhibiting IL-12 prodn. by macrophages and dendritic  
cells and (ii) modulating M. tuberculosis-induced macrophage apoptosis.  
RE.CNT 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 10 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 5  
AN 2002:303338 CAPLUS  
DN 137:288700  
TI Differential modulation of apoptosis and necrosis by antioxidants in  
immunosuppressed human lymphocytes  
AU \*\*\*Rojas, Mauricio\*\*\* ; Rugeles, Maria Teresa; Gil, Diana Patricia;  
Patino, Pablo  
CS Grupo de Inmunologia Celular e Inmunogenetica, Laboratorio Central de  
Investigaciones, Universidad de Antioquia, Medellin, Colombia  
SO Toxicology and Applied Pharmacology (2002), 180(2), 67-73  
CODEN: TXAPAP9; ISSN: 0041-008X  
PB Elsevier Science  
DT Journal  
LA English  
AB In the present study, the authors explored whether mitogenic stimulation  
of dexamethasone (DXM)- and cyclosporine A (CsA)-immunosuppressed  
peripheral blood lymphocytes (PBML) induced apoptosis or necrosis and  
their relation with the prodn. of reactive oxygen intermediates. The  
authors' results indicate that both phenomena can occur in these cells and

that antioxidants such as N-acetyl Cys (NAC) and ascorbic acid (AA) can modulate them. However, DXM-induced apoptosis was only partially inhibited by NAC and AA, suggesting that DXM-treated PBMC had an addnl. apoptotic pathway independent of ROIs. Furthermore, the authors obsd. that the inhibition of apoptosis by antioxidants correlated with an increased cell proliferation, suggesting that the immunomodulation of both DXM and CsA may be related to induction of apoptosis. The ability to differentially modulate apoptosis and necrosis by antioxidants opens new possibilities in the management of immunosuppressive therapy, since the inhibition of necrosis may avoid inflammation and the tissue damage assocd. with immunosuppressors.

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 11 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 6  
AN 2002:843818 CAPLUS  
DN 138:54470  
TI Activation of JAK2/STAT1-.alpha.-dependent signaling events during Mycobacterium tuberculosis-induced macrophage apoptosis  
AU \*\*\*Rojas, Mauricio\*\*\* ; Olivier, Martin; Garcia, Luis F.  
CS Grupo de Inmunologia Celular e Inmunogenetica, Facultad de Medicina, Universidad de Antioquia, Medellin, Colombia  
SO Cellular Immunology (2002), 217(1/2), 58-66  
CODEN: CLIMB8; ISSN: 0008-8749  
PB Elsevier Science  
DT Journal  
LA English  
AB Induction of apoptosis by Mycobacterium tuberculosis in murine macrophage involves TNF-.alpha. and nitric oxide (NO) prodn. and caspase cascade activation; however, the intracellular signaling pathways implicated remain to be established. The authors' results indicate that infection of the B10R murine macrophage line with M. tuberculosis induces apoptosis independent of mycobacterial phagocytosis and that M. tuberculosis induces protein tyrosine kinase (PTK) activity, JAK2/STAT1-.alpha. phosphorylation, and STAT1-.alpha. nuclear translocation. Inhibitors of PTK (AG-126), or JAK2 (AG-490) inhibited TNF-.alpha. and NO prodn., caspase 1 activation and apoptosis, suggesting that M. tuberculosis-induction of these events depends on JAK2/STAT1-.alpha. activation. In addn., the authors have obtained evidence that ManLAM capacity to inhibit M. tuberculosis-induced apoptosis involves the activation of the PTP SHP-1. The finding that M. tuberculosis infection activate JAK2/STAT1-.alpha. pathway suggests that M. tuberculosis might mimic macrophage-activating stimuli.

RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 12 OF 31 USPATFULL on STN  
AN 2001:93325 USPATFULL  
TI Sequence and method for genetic engineering of proteins with cell membrane translocating activity  
IN Lin, Yao-Zhong, Nashville, TN, United States  
Donahue, John P., Nashville, TN, United States  
\*\*\*Rojas, Mauricio\*\*\* , Nashville, TN, United States  
Tan, Zhong-Jia, Nashville, TN, United States  
PA Vanderbilt University, Nashville, TN, United States (U.S. corporation)  
PI US 6248558 B1 20010619  
AI US 1998-186170 19981104 (9)  
PRAI US 1998-80083P 19980331 (60)  
DT Utility  
FS GRANTED  
EXNAM Primary Examiner: Carlson, Karen Cochrane; Assistant Examiner: Srivastava, Devesh  
LREP Needle & Rosenberg, P.C.  
CLMN Number of Claims: 32  
ECL Exemplary Claim: 1  
DRWN 15 Drawing Figure(s); 9 Drawing Page(s)  
LN.CNT 1376  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB The invention describes a membrane-translocating peptide sequence (MTS) which facilitates entry of polypeptides and proteins into cells. Also described is an isolated nucleotide sequence encoding the

membrane-translocating peptide and a method of using this sequence to genetically engineer proteins with cell membrane permeability. The MTS, and the method of genetically engineering proteins with cell membrane permeability, are useful for polypeptide and protein delivery for human and veterinary applications such as vaccine delivery and cancer therapy.

L2 ANSWER 13 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2001:832547 CAPLUS  
DN 136:117228  
TI Cutting edge: B cell specificity contributes to the outcome of diabetes in nonobese diabetic mice  
AU Hulbert, Chrys; Riseili, Brent; \*\*\*Rojas, Mauricio\*\*\* ; Thomas, James W.  
CS Departments of Medicine, Microbiology and Immunology, Vanderbilt University, Nashville, TN, 37232, USA  
SO Journal of Immunology (2001), 167(10), 5535-5538  
CODEN: JOIMA3; ISSN: 0022-1767  
PB American Association of Immunologists  
DT Journal  
LA English  
AB Type I diabetes mellitus (T1DM) is an autoimmune disorder characterized by T cell-mediated destruction of insulin-producing beta cells in the pancreas. In the nonobese diabetic (NOD) model of T1DM, insulitis and diabetes are dependent on the presence of B lymphocytes; however, the requirement for specificity within the B cell repertoire is not known. To det. the role of antigen-specific B cells in T1DM, VH genes with different potential for insulin binding were introduced into NOD as H chain transgenes. VH125 H chain combines with endogenous L chains to produce a repertoire in which 1-3% of mature B cells are insulin specific, and these mice develop accelerated diabetes. In contrast, NOD mice harboring a similar transgene, VH281, with limited insulin binding develop insulitis but are protected from T1DM. Thus, antigen-specific components in the B cell repertoire may alter the course of T1DM.

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 14 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2001:167084 CAPLUS  
DN 134:325153  
TI Anergy and not clonal ignorance determines the fate of B cells that recognize a physiological autoantigen  
AU \*\*\*Rojas, Mauricio\*\*\* ; Hulbert, Chrys; Thomas, James W.  
CS Department of Medicine, Division of Rheumatology and Immunology, Vanderbilt University, Nashville, TN, 37232, USA  
SO Journal of Immunology (2001), 166(5), 3194-3200  
CODEN: JOIMA3; ISSN: 0022-1767  
PB American Association of Immunologists  
DT Journal  
LA English  
AB Autoantibodies to insulin arise spontaneously in the insulin autoimmune syndrome and in type I diabetes. In addn., administration of insulin to individuals without autoimmune disease routinely results in Abs that bind autologous hormone. These observations and findings in transgenic models of tolerance led to an inference that physiol. levels of hormones and growth factors, such as insulin, are not sufficient to induce tolerance in B cells, a state termed clonal ignorance. In contrast, the authors have discovered that virtually all conventional B cells expressing a low affinity anti-insulin transgene interact with endogenous insulin and are effectively silenced for Ig prodn. and for T cell-dependent immune responses. A fraction of transgenic B cells escapes silencing and functions autonomously to produce insulin Abs that may lower fasting blood sugars similar to an insulin autoimmune syndrome. These B cells have characteristics of a B1-like subset and are depleted by hypotonic peritoneal lysis. These findings question the concept of clonal ignorance and show that physiol. concns. of Ag may effectively silence conventional B cells even when the affinity for autoantigen is low. Self-reactivity may arise in the repertoire because of compartmental differences that govern the fate of B cells and not as a result of true clonal ignorance.

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 15 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2000:588350 CAPLUS  
 DN 134:146340  
 TI Mannosylated lipoarabinomannan antagonizes *Mycobacterium*  
 tuberculosis-induced macrophage apoptosis by altering Ca<sup>2+</sup>-dependent cell  
 signaling  
 AU \*\*\*Rojas, Mauricio\*\*\* ; Garcia, Luis F.; Nigou, Jerome; Puzo, Germain;  
 Olivier, Martin  
 CS Grupo de Inmunología Celular e Inmunogenética. Laboratorio Central de  
 Investigaciones, Centro de Investigaciones Médicas, Facultad de Medicina.  
 Universidad de Antioquia, Medellín, AA 1226, Colombia  
 SO Journal of Infectious Diseases (2000), 182(1), 240-251  
 CODEN: JIDIAQ; ISSN: 0022-1899  
 PB University of Chicago Press  
 DT Journal  
 LA English  
 AB *Mycobacterium* tuberculosis-induced macrophage apoptosis can be inhibited  
 by mannosylated lipoarabinomannan (ManLAM), although it induces tumor  
 necrosis factor (TNF)-.alpha. and NO prodn., which participate in  
 apoptosis induction. ManLAM also modulates Ca<sup>2+</sup>-dependent intracellular  
 events, and Ca<sup>2+</sup> participates in apoptosis in different systems. Ca<sup>2+</sup> was  
 assessed for involvement in *M. tuberculosis*-induced macrophage apoptosis  
 and for modulation by ManLAM. The role of Ca<sup>2+</sup> was supported by the  
 blockade of apoptosis by cAMP inhibitors and the Ca<sup>2+</sup> chelator, BAPTA/AM.  
 These agents also inhibited caspase-1 activation and cAMP-responsive  
 element-binding protein translocation without affecting TNF-.alpha. prodn.  
 Infection of macrophages with *M. tuberculosis* induced an influx of Ca<sup>2+</sup>  
 that was prevented by ManLAM. Similarly, *M. tuberculosis*  
 infection-altered mitochondrial permeability transition was prevented by  
 ManLAM and BAPTA/AM. Finally, ManLAM and BAPTA/AM reversed the effects of  
*M. tuberculosis* on p53 and Bcl-2 expression. ManLAM counteracts the  
 alterations of calcium-dependent intracellular events that occur during *M.*  
 tuberculosis-induced macrophage apoptosis.

RE.CNT 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 16 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1999:640717 CAPLUS  
 DN 131:267937  
 TI Membrane-translocating peptide MTS and method for genetic engineering of  
 proteins with cell membrane translocating activity  
 IN Lin, Yao-zhong; Donahue, John P.; \*\*\*Rojas, Mauricio\*\*\* ; Tan, Zhong  
 Jia  
 PA Vanderbilt University, USA  
 SO PCT Int. Appl., 85 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9949879	A1	19991007	WO 1999-US7189	19990331
	W: AU, CA, JP				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 6248558	B1	20010619	US 1998-186170	19981104
	AU 9934628	A1	19991018	AU 1999-34628	19990331
	EP 1067949	A1	20010117	EP 1999-916273	19990331
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 6432680	B1	20020813	US 2000-562868	20000501
	US 2002143142	A1	20021003	US 2002-116288	20020404
	US 6780843	B2	20040824		
PRAI	US 1998-80083P	P	19980331		
	US 1998-186170	A	19981104		
	WO 1999-US7189	W	19990331		
	US 2000-562868	A3	20000501		
AB	The invention describes a membrane-translocating peptide sequence (MTS) which facilitates entry of polypeptides and proteins into cells. Also described is an isolated nucleotide sequence encoding the membrane-translocating peptide and a method of using this sequence to				

genetically engineer proteins with cell membrane permeability. The MTS, and the method of genetically engineering proteins with cell membrane permeability, are useful for polypeptide and protein delivery for human and veterinary applications such as vaccine delivery and cancer therapy.

L2 ANSWER 17 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1999:329699 CAPLUS  
DN 131:115185  
TI TNF-.alpha. and IL-10 modulate the induction of apoptosis by virulent *Mycobacterium tuberculosis* in murine macrophages  
AU \*\*\*Rojas, Mauricio\*\*\* ; Olivier, Martin; Gros, Philippe; Barrera, Luis F.; Garcia, Luis F.  
CS Grupo de Inmunologia Celular e Inmunogenetica, Laboratorio Central de Investigaciones, Centro de Investigaciones Medicas, Facultad de Medicina, Universidad de Antioquia, Medellin, Colombia  
SO Journal of Immunology (1999), 162(10), 6122-6131  
CODEN: JOIMA3; ISSN: 0022-1767  
PB American Association of Immunologists  
DT Journal  
LA English  
AB The *Bcg/Nramp1* gene controls early resistance and susceptibility of macrophages to mycobacterial infections. The authors previously reported that *M. tuberculosis*-infected (Mtb) B10R (*Bcgr*) and B10S (*Bcgs*) macrophages differentially produce nitric oxide (NO-), leading to macrophage apoptosis. Since TNF-.alpha. and IL-10 have opposite effects on many macrophage functions, the authors detd. the no. of cells producing TNF-.alpha. and IL-10 in Mtb-infected or purified protein deriv.-stimulated B10R and B10S macrophages lines, and *Nramp1*+/+ and *Nramp1*-/- peritoneal macrophages and correlated them with Mtb-mediated apoptosis. Mtb infection and purified protein deriv. treatment induced more TNF-.alpha.+*Nramp1*+/+ and B10R, and more IL-10+*Nramp1*-/- and B10S cells. Treatment with mannosylated lipoarabinomannan, which rescues macrophages from Mtb-induced apoptosis, augmented the no. of IL-10 B10R+ cells. Anti-TNF-.alpha. inhibited apoptosis, diminished NO- prodn., p53, and caspase 1 activation and increased Bcl-2 expression. In contrast, anti-IL-10 increased caspase 1 activation, p53 expression, and apoptosis, although there was no increment in NO- prodn. Murine rTNF-.alpha. induced apoptosis in noninfected B10R and B10S macrophages that was reversed by murine rIL-10 in a dose-dependent manner with concomitant inhibition of NO- prodn. and caspase 1 activation. NO- and caspase 1 seem to be independently activated in that aminoguanidine did not affect caspase 1 activation and the inhibitor of caspase 1, Tyr-Val-Ala-Asp-acyclooxymethylketone, did not block NO- prodn.; however, both treatments inhibited apoptosis. Thus, Mtb activates TNF-.alpha.- and IL-10-dependent opposite signals in the induction of macrophage apoptosis and the TNF-.alpha./IL-10 ratio is controlled by the *Nramp1* background of resistance/susceptibility and may account for the balance between apoptosis and macrophage survival.

RE.CNT 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 18 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1999:396728 CAPLUS  
DN 131:209296  
TI Application of cell-permeable peptides to the functional analysis of EGF-induced mitogenic signaling pathways  
AU \*\*\*Rojas, Mauricio\*\*\* ; Yao, SongYi; Donahue, John P.; Lin, Yao-Zhong  
CS Department of Microbiology and Immunology, Vanderbilt University, Nashville, TN, 37232, USA  
SO Peptides: Frontiers of Peptide Science, Proceedings of the American Peptide Symposium, 15th, Nashville, June 14-19, 1997 (1999), Meeting Date 1997, 733-734. Editor(s): Tam, James P.; Kaumaya, Pravin T. P. Publisher: Kluwer, Dordrecht, Neth.  
CODEN: 67UCAR  
DT Conference  
LA English  
AB To det. the functional consequence of disrupting the EGFR/Grb2 or Shc/Grb2 protein-protein assocns. in vivo, the authors delivered peptides contg. either the EGFR Tyr1068 or the Shc Tyr 317-contg. region into intact cells using a nondestructive cell-permeable peptide import method. To influence EGF-induced EGFR/Grb2 interaction, the authors designed a peptide

comprised of a cell permeable sequence at its N-terminus (underlined) and the phosphotyrosine 1068-contg. site of EGFR at its C-terminus, AAVALLPVALLAPLPVPEpYINQSV (SP1068 peptide). In EGF-stimulated SAA cells (NIH 3T3 cells overexpressing EGFR), the phosphorylated EGFR was copptd. with Grb2. However, the amt. of assocd. EGFR was significantly reduced in cells pretreated with SP1068 peptide. Neither non-cell permeable P1068 nor cell-permeable unphosphorylated SY1068 peptide treatment showed any significant inhibition. Peptide-mediated disruption of the EGFR/Grb2/Sos-1 cascade led to reduced Ras activation and MAP kinase activation in EGF-stimulated cells. The authors also delivered cell-permeable peptides carrying Shc Tyr317-contg. region into SAA cells, AAVALLPVALLAPFDDPSYVNQNL. The EGF-induced Shc/Grb2 assocn. was inhibited substantially in the cells treated with phosphorylated SP317 peptide. Interestingly, this assocn. was also inhibited by unphosphorylated SY317 peptide. In contrast, the non-cell-permeable Shc peptide (P317) and cell-permeable SY1068 peptide were without significant effect. To verify that the Grb2-binding activities of non-phosphorylated SY317 peptide do not result from in vivo phosphorylation of the peptide, the authors used an in vitro peptide-protein binding assay. Results showed that Grb2 SH2 protein could bind both phosphorylated and unphosphorylated Shc peptides, but not an unphosphorylated SY1068 peptide derived from the EGFR. This finding represents the first paradigm of the functional interaction between an unphosphorylated tyrosine-contg. motif and an SH2 domain.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 19 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1998:420791 CAPLUS  
DN 129:147988  
TI Induction of apoptosis in murine macrophages by *Mycobacterium tuberculosis* is reactive oxygen intermediates-independent  
AU \*\*\*Rojas, Mauricio\*\*\* ; Barrera, Luis F.; Garcia, Luis F.  
CS Grupo de Inmunologia Celular e Inmunogenetica, Laboratorio Central de Investigaciones, Facultad de Medicina, Universidad de Antioquia, Medellin, Colombia  
SO Biochemical and Biophysical Research Communications (1998), 247(2), 436-442  
CODEN: BBRCA9; ISSN: 0006-291X  
PB Academic Press  
DT Journal  
LA English  
AB Infection with *M. tuberculosis* induces apoptosis in murine macrophage lines. Resistant macrophages B10R (Bcgr) are more prone to undergo apoptosis than susceptible B10S (Bcgs) macrophages. Apoptosis and inhibition of intracellular growth of the mycobacteria seem to be dependent on the prodn. of nitric oxide, since both can be reverted by aminoguanidine (AMG). Although B10R macrophages produce more superoxide anion than B10S macrophages after infection with *M. tuberculosis*, reactive oxygen intermediate (ROIs) scavengers did not affect uptake of 3H-uracil incorporation by the mycobacteria nor the induction of apoptosis. These results further suggest that both phenomena are dependent on the prodn. of nitric oxide by the infected macrophages. (c) 1998 Academic Press.

RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 20 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1998:240574 CAPLUS  
DN 129:24701  
TI Genetic engineering of proteins with cell membrane permeability  
AU \*\*\*Rojas, Mauricio\*\*\* ; Donahue, John P.; Tan, Zhongjia; Lin, Yao-Zhong  
CS Department of Microbiology and Immunology, Vanderbilt Univ., Nashville, TN, 37232, USA  
SO Nature Biotechnology (1998), 16(4), 370-375  
CODEN: NABIF9; ISSN: 1087-0156  
PB Nature America  
DT Journal  
LA English  
AB The discovery of methods for generating proteins with inherent cell membrane-translocating activity will expand our ability to study and manipulate various intracellular processes in living systems. We report a

method to engineer proteins with cell-membrane permeability. After a 12-amino acid residue membrane-translocating sequence (MTS) was fused to the C-terminus of glutathione S-transferase (GST), the resultant GST-MTS fusion proteins were efficiently imported into NIH 3T3 fibroblasts and other cells. MTS has the amino acid sequence AAVLLPVLLAAP. To explore the applicability of this nondestructive important method to the study of intracellular processes, a 41-kDa GST-Grb2SH2-MTS fusion protein contg. the Grb2 SH2 domain was tested for its effect on the epidermal growth factor (EGF)-stimulated signaling pathway. This fusion protein entered cells, formed a complex with phosphorylated EGF receptor (EGFR), and inhibited EGF-induced EGFR-Grb2 assocn. and mitogen-activated protein kinase activation.

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 21 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1998:133304 CAPLUS  
DN 128:291642  
TI Conformational and topological requirements of cell-permeable peptide function  
AU Du, Caigan; Yao, Songyi; \*\*\*Rojas, Mauricio\*\*\* ; Lin, Yao-Zhong  
CS Department of Microbiology and Immunology, Vanderbilt University School of Medicine, Nashville, TN, USA  
SO Journal of Peptide Research (1998), 51(3), 235-243  
CODEN: JPERFA; ISSN: 1397-002X  
PB Munksgaard International Publishers Ltd.  
DT Journal  
LA English  
AB Cell-permeable peptide import recently was developed to deliver synthetic peptides into living cells for studying intracellular protein functions. This import process is mediated by an N-terminal carrier sequence which is the hydrophobic region of a signal peptide. In this study, the conformational consequence of the interaction of cell-permeable peptides with different mimetic membrane environments was investigated by CD anal. We showed that cell-permeable peptides adopted .alpha.-helical structures in sodium dodecyl sulfate (SDS) micelles or aq. trifluoroethanol (TFE). The potency of these peptides in forming helical structures is higher in an amphiphilic environment (SDS) than in a hydrophobic environment (TFE), suggesting that some hydrophilic mols. assocd. with the cell membrane may be involved in peptide import. We also studied topol. requirements of cell-permeable peptide function. We demonstrated that peptides contg. the carrier sequence in their C-termini can also be imported into cells efficiently. This important discovery can avoid repetitious synthesis of the membrane-translocating sequence for peptides with different functional cargoes and is potentially useful for developing a cell-permeable peptide library. Finally, we showed that, when a retro version of the carrier sequence was used, the peptide lost its translocating ability despite retaining a high content of .alpha.-helical structure in mimetic membrane environments. This suggests that the propensity of peptides to adopt a helical conformation is required but not sufficient for cellular import and that other structural factors such as the side-chain topol. of the carrier sequence are also important. Our studies together contribute to the more rational design of useful cell-permeable peptides.

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 22 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1997:777924 CAPLUS  
DN 128:60644  
TI Inhibition of virulent Mycobacterium tuberculosis by Bcgr and Bcgs macrophages correlates with nitric oxide production  
AU Arias, Mauricio; \*\*\*Rojas, Mauricio\*\*\* ; Zabaleta, Jovanny; Rodriguez, Jaime I.; Paris, Sara C.; Barrera, Luis F.; Garcia, Luis F.  
CS Laboratorio Central de Investigaciones, Facultad de Medicina, Universidad de Antioquia, Medellin, Colombia  
SO Journal of Infectious Diseases (1997), 176(6), 1552-1558  
CODEN: JIDIAQ; ISSN: 0022-1899  
PB University of Chicago Press  
DT Journal  
LA English  
AB The Nramp1 gene controls macrophage resistance or susceptibility to

several intracellular microorganisms; however, there is conflicting evidence regarding its role during infection with virulent *Mycobacterium tuberculosis*. Nitric oxide (NO) is a potent antimycobacterial agent produced by macrophages, which is also regulated by Nrampl. The in vitro ability of B10R (resistant) and B10S (susceptible) murine macrophages to inhibit *M. tuberculosis* H37Rv and to produce NO in response to infection and interferon- $\gamma$  (IFN- $\gamma$ ) was compared. Infected B10R macrophages inhibited [<sup>3</sup>H]uracil incorporation by *M. tuberculosis* and produced higher amounts of NO than did B10S macrophages. IFN- $\gamma$  increased the inhibitory activity of both cells. Inhibition of *M. tuberculosis* by IFN- $\gamma$ -activated B10R macrophages was reversed by NG-monomethyl-L-arginine (NGMMA). L-Arginine restored NO prodn. and increased the antimycobacterial activity by IFN- $\gamma$ -stimulated NGMMA-treated macrophages. The Bcg/Nrampl gene may regulate macrophage resistance or susceptibility to virulent *M. tuberculosis* by a differential capability of these cells to produce NO.

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 23 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1997:476510 CAPLUS  
DN 127:204321  
TI Differential induction of apoptosis by virulent *Mycobacterium tuberculosis* in resistant and susceptible murine macrophages. Role of nitric oxide and mycobacterial products  
AU \*\*\*Rojas, Mauricio\*\*\* ; Barrera, Luis F.; Puzo, Germain; Garcia, Luis F.  
CS Lab. Central Investigaciones, Centro Investigaciones Medicas, Facultad Medicina, Univ. Antioquia, Medellin, Colombia  
SO Journal of Immunology (1997), 159(3), 1352-1361  
CODEN: JOIMA3; ISSN: 0022-1767  
PB American Association of Immunologists  
DT Journal  
LA English  
AB Resistance and susceptibility and macrophages to mycobacteria are under the control of the Bcg/Nrampl gene, which also controls the NO $^-$  (nitric oxide) prodn. in response to macrophage activators. There is recent evidence indicating that mycobacteria induces apoptosis in infected macrophages. Using murine macrophage lines, congenic at the Bcg/Nrampl genes, this report shows that B10R are more prone than B10S macrophages to undergo apoptosis after exposure to live virulent *Mycobacterium tuberculosis* H37Rv (Mtb) or PPD, as detd. by cell viability, DNA fragmentation, hypoploidy, and the terminal deoxynucleotide transferase dUTP-biotin nick-end labeling assay. Induction of apoptosis correlated with NO $^-$  prodn. Aminoguanidine and anti-TNF- $\alpha$ - inhibited NO $^-$  prodn. and apoptosis. B10R and B10S macrophages were equally affected by sodium nitroprusside, a donor of NO $^-$ , but its effect, mainly in B10R cells, was enhanced by the presence of Mtb. Nonvirulent mycobacteria induced lower levels of NO $^-$  and did not cause cell death. Killed Mtb, mannose-capped lipoarabinomannan (ManLAM), and LPS rescued macrophages from apoptosis albeit induce NO $^-$ . These findings suggest that existence of opposite pathways: metabolically active mycobacteria promotes apoptosis whereas their structural components inhibit it. Apoptosis may be a crit. mechanism by which Nrampl gene controls the macrophage infection with virulent mycobacteria.

RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 24 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1997:381685 CAPLUS  
DN 127:105781  
TI An alternative to phosphotyrosine-containing motifs for binding to an SH2 domain  
AU \*\*\*Rojas, Mauricio\*\*\* ; Yao, SongYi; Donahue, John P.; Lin, Yao-Zhong  
CS Dep. Microbiol. Immunol., Vanderbilt Univ. Sch. Med., Nashville, TN, 37232-2363, USA  
SO Biochemical and Biophysical Research Communications (1997), 234(3), 675-680  
CODEN: BBRCA9; ISSN: 0006-291X  
PB Academic  
DT Journal

LA English  
AB Shc is an important signaling protein whose overexpression leads to cell transformation in NIH 3T3 fibroblasts. Although the formation of Shc/Grb2 complexes involving Shc tyrosine residue 317 is necessary to induce this transformation, the Shc proteins in these Shc-overexpressing cells are not substantially tyrosine-phosphorylated. This observation led to our hypothesis that the non-phosphorylated Tyr317-contg. region of Shc might have specific affinity for the Grb2 protein. We show here that cell-permeable peptides encompassing the Shc Tyr317 region, 312FDDPSYVNVQNL323, can bind to the SH2 domain of Grb2 regardless of the state of tyrosine phosphorylation. When delivered into cells, both phosphorylated and non-phosphorylated Shc peptides inhibit growth factor-induced Shc/Grb2 protein-protein interaction. The non-phosphorylated Shc peptides with single point mutations at Asp313, Asp314, or Tyr317 are inactive, suggesting that these residues play an important role in Grb2 protein recognition. Our findings represent the first paradigm of the specific interaction between an unphosphorylated tyrosine-contg. region and an SH2 domain and have important implications for understanding the mechanism of cell transformation by Shc overexpression.

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 25 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1996:681566 CAPLUS  
DN 126:1643  
TI Controlling epidermal growth factor (EGF)-stimulated Ras activation in intact cells by a cell-permeable peptide mimicking phosphorylated EGF receptor  
AU \*\*\*Rojas, Mauricio\*\*\* ; Yao, SongYi; Lin, Yao-Zhong  
CS Department Microbiology Immunology, Vanderbilt University School Medicine, Nashville, TN, 37232-2363, USA  
SO Journal of Biological Chemistry (1996), 271(44), 27456-27461  
CODEN: JBCHA3; ISSN: 0021-9258  
PB American Society for Biochemistry and Molecular Biology  
DT Journal  
LA English  
AB EGF-stimulated Ras activation involves specific interactions between the EGF receptor (EGFR), the adaptor proteins Grb2 and Shc, and the nucleotide exchange factor Sos-1. Study and control of these protein-protein interactions in vivo can be greatly promoted by introducing intracellular reagents that mimic EGFR functions. Here, the authors showed that a synthetic phosphopeptide encompassing the autophosphorylation site 1068 of EGFR formed a complex with endogenous Grb2 after this peptide was delivered into intact cells by a cell-permeable peptide import technique. Consequently, this intracellular peptide inhibited EGF-induced EGFR/Grb2 assocns. but not EGFR/Shc or Shc/Grb2 assocns. Peptide-mediated disruption of the EGF/Grb2/Sos-1 cascade led to reduced Ras activation and mitogen-activated protein kinase activation. These results indicate that the binding of Grb2 to the phosphorylated Tyr-1068 of EGFR is crucial to the EGF-induced Ras/mitogen-activated protein kinase signaling pathway. The application of cell-permeable peptides to this study demonstrates a useful biochem. tool to this study demonstrates a useful biochem. tool to probe and control various intracellular processes involved in signal transduction and gene transcription.

L2 ANSWER 26 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1994:534561 CAPLUS  
DN 121:134561  
TI Unambiguous 13C NMR assignment of acnistins and absolute configuration of acnistin A  
AU Gutierrez Luis, Javier; Echeverri, Fernando; Quinones, Winston; Gonzalez, Antonio G.; Torres, Fernando; Cardona, Gloria; Archbold, Rodendo;  
\*\*\*Rojas, Mauricio\*\*\* ; Perales, Aurea  
CS Inst. Bioorg., Univ. La Laguna, La Laguna, 38206, Spain  
SO Steroids (1994), 59(5), 299-304  
CODEN: STEDAM; ISSN: 0039-128X  
DT Journal  
LA English  
AB Carbon and proton atoms were fully assigned in a new type of withanolide by HMQC and HMBC expts. The abs. configuration of acnistin A (I) was

dtd. by x-ray diffraction. Proton and <sup>13</sup>C NMR measurements are particularly useful in identifying members of this group of natural products.

L2 ANSWER 27 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1993:491270 CAPLUS  
DN 119:91270  
TI Irenolone and emenolone: two new types of phytoalexin from *Musa paradisiaca*  
AU Luis, Javier G.; Echeverri, Fernando; Quinones, Winston; Brito, Ivan; Lopez, Matias; Torres, Fernando; Cardona, Gloria; Aguiar, Zahira; Pelaez, Carlos; \*\*\*Rojas, Mauricio\*\*\*  
CS Inst. Bio-Org., Univ. La Laguna, La Laguna, 38206, Spain  
SO Journal of Organic Chemistry (1993), 58(16), 4306-8  
CODEN: JOCEAH; ISSN: 0022-3263  
DT Journal  
LA English  
AB Phenalenone-type phytoalexins were obtained for the first time from bananas and identified by COSY 1H-1H, HMQC and HMBC techniques, and X-ray anal., among other methods. The aminoglycoside kanamycin was studied as a phytoalexin inducer in banana leaves and fruit and compared with the effects produced by the fungus *Mycosphaerella fijiensis*. The Ph side chain in banana phytoalexins is not in the same position as in other plant phenalenones and so an alternative biogenetic pathway has been proposed and verified. The specific response evoked by kanamycin opens the way to the study of the host-plant relationship from a new angle since more phytoalexin inducers can be designed on the basis of the chem. constituents of the microorganisms involved or on synthetic kanamycin analogs and used to improve the plants' defense mechanisms.

L2 ANSWER 28 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1993:533407 CAPLUS  
DN 119:133407  
TI Larvicidal activity of 7-methoxyaromadendrin against *Culex* sp. larvae  
AU Echeverri, Fernando; Torres, Fernando; Cardona, Gloria; Lopez, Jairo; Quinones, Winston; Gallego, Luis H.; Pelaez, Carlos A.; \*\*\*Rojas,\*\*\*  
\*\*\* Mauricio\*\*\* ; Garcia, Fernando; Restrepo, Luz Marina  
CS Dep. Quim., Univ. Antioquia, Medellin, Colombia  
SO Revista Boliviana de Quimica (1992), 11(1), 43-5  
CODEN: RBQUDX; ISSN: 0250-5460  
DT Journal  
LA Spanish  
AB At 250 ppm the dihydroflavonol 7-methoxyaromadendrin (extd. from *Eucalyptus tereticornis* resin) was highly larvicidal (24 h) to *Culex* mosquitoes. Moderate mortality was obtained at 125 ppm. Problems assocd. with the solv. of 7-methoxyaromadendrin are discussed.

L2 ANSWER 29 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1993:513602 CAPLUS  
DN 119:113602  
TI Phytoalexins in diseased tree tomato fruit and their antibiotic activity  
AU Echeverri, Fernando; Torres, Fernando; Cardona, Gloria; Lopez, Jairo; Quinones, Winston; Gallego, Luis H.; Pelaez, Carlos A.; \*\*\*Rojas,\*\*\*  
\*\*\* Mauricio\*\*\* ; Garcia, Fernando; Restrepo, Luz Marina  
CS Dep. Quim., Univ. Antioquia, Medellin, Colombia  
SO Revista Boliviana de Quimica (1992), 11(1), 39-41  
CODEN: RBQUDX; ISSN: 0250-5460  
DT Journal  
LA Spanish  
AB Two phytoalexins were isolated from fruit of tree tomato (*Cyphomandra betacea*) infected by *Colletotrichum gloeosporioides*. One of the phytoalexins (benzoic acid) was very active against the pathogen.

L2 ANSWER 30 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1992:508124 CAPLUS  
DN 117:108124  
TI Isolation of an ingestion deterrent from *Passiflora foetida* L  
AU Echeverri, Fernando; Torres, Fernando; Cardona, Gloria; Lopez, Jairo; Quinones, Winston; Gallego, Luis H.; Pelaez, Carlos; \*\*\*Rojas,\*\*\*  
\*\*\* Mauricio\*\*\* ; Garcia, Fernando; Restrepo, Luz Marina  
CS Dep. Quim., Univ. Antioquia, Medellin, Colombia

SO Revista Boliviana de Quimica (1991), 10(1), 25-9  
CODEN: RBQUDX; ISSN: 0250-5460  
DT Journal  
LA Spanish  
AB Ten flavonoids were isolated from the resin of *P. foetida*. One of them, ermanin, showed a strong feeding deterrent activity toward *Dione juno* larvae.  
  
L2 ANSWER 31 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1992:466651 CAPLUS  
DN 117:66651  
TI Withajardines: structure and activity  
AU Echeverri, Fernando; Torres, Fernando; Cardona, Gloria; Lopez, Jairo; Quinones, Winston; Gallego, Luis H.; Pelaez, Carlos; \*\*\*Rojas,\*\*\*  
\*\*\* Mauricio\*\*\* ; Garcia, Fernando; Restrepo, Luz Marina  
CS Dep. Quim., Univ. Antioquia, Medellin, Colombia  
SO Revista Boliviana de Quimica (1991), 10(1), 21-3  
CODEN: RBQUDX; ISSN: 0250-5460  
DT Journal  
LA Spanish  
AB Withajardin A and withajardin B were isolated from *Deprea orinocensis* leaves. Their structures were identified by spectral and chem. data. The compds. showed immunosuppressant and activities.

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E1 1 MORA ALVAREZ YUNUEN GUADALUPE/AU  
E2 5 MORA AMERIGO E/AU  
E3 4 --> MORA ANA/AU  
E4 23 MORA ANA L/AU  
E5 1 MORA ANA LUCIA/AU  
E6 1 MORA ANACLETO/AU  
E7 1 MORA ANDRE/AU  
E8 2 MORA ANDRES/AU  
E9 1 MORA ANDRES E/AU  
E10 1 MORA ANDRES ELOY/AU  
E11 1 MORA ANGELA L/AU  
E12 1 MORA ANGELA MARIA MOYA/AU  
  
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L4 21 DUP REM L3 (7 DUPLICATES REMOVED)

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YOU HAVE REQUESTED DATA FROM 21 ANSWERS - CONTINUE? Y/(N):y

L4 ANSWER 1 OF 21 MEDLINE on STN  
AN 2005013057 IN-PROCESS  
DN PubMed ID: 15475380  
TI Endotoxin-induced lung injury in mice: structural, functional, and biochemical responses.  
AU Rojas Mauricio; Woods Charles R; \*\*\*Mora Ana L\*\*\* ; Xu Jianguo; Brigham Kenneth L  
CS Division of Pulmonary, Allergy and Critical Care, Center for Translational Research of the Lung, Emory University School of Medicine, Atlanta, GA 30322, USA.. mrojas@emory.edu  
NC 5 P01 HL-0669496-02 (NHLBI)  
SO American journal of physiology. Lung cellular and molecular physiology, (2005 Feb) 288 (2) L333-41.  
Journal code: 100901229. ISSN: 1040-0605.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS IN-PROCESS; NONINDEXED; Priority Journals  
ED Entered STN: 20050111  
Last Updated on STN: 20050126  
AB Acute lung injury is usually a complication of sepsis, and endotoxin treatment of mice is a frequently used experimental model. To define this

model and to clarify pathogenesis of the lung injury, we injected with 1 mg/kg endotoxin ip and measured pulmonary function, pulmonary edema, serum concentrations of cytokines and growth factors, and lung histology over 48 h. During the first 6 h, tidal volume and minute volume increased and respiratory frequency decreased. Serum concentrations of cytokines showed three patterns: 10 cytokines peaked at 2 h and declined rapidly, two peaked at 6 h and declined, and two had biphasic peaks at 2 and 24 h. Growth factors increased later and remained elevated longer. Both collagen and fibronectin were deposited in the lungs beginning within hours of endotoxin and resolving over 48 h. Histologically, lungs showed increased cellularity at 6 h with minimal persistent inflammation at 48 h. Lung water peaked at 6 h and gradually decreased over 48 h. We conclude that intraperitoneal administration of endotoxin to mice causes a transient systemic inflammatory response and transient lung injury and dysfunction. The response is characterized by successive waves of cytokine release into the circulation, early evidence of lung fibrogenesis, and prolonged increases in growth factors that may participate in lung repair.

L4 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1  
AN 2004:771553 CAPLUS  
DN 141:348504  
TI An IL-4R.alpha. Allelic Variant, I50, Acts as a Gain-of-Function Variant Relative to V50 for Stat6, But Not Th2 Differentiation  
AU Stephenson, Linda; Johns, Mary H.; Woodward, Emily; \*\*\*Mora, Ana L.\*\*\* ; Boothby, Mark  
CS Department of Microbiology and Immunology, Vanderbilt University Medical School, Nashville, TN, 37232, USA  
SO Journal of Immunology (2004), 173(7), 4523-4528  
CODEN: JOIMA3; ISSN: 0022-1767  
PB American Association of Immunologists  
DT Journal  
LA English  
AB Signaling through the IL-4R .alpha.-chain (IL-4R.alpha.) is crucial for the development of Th2 cells, central effectors in atopic disease. Alleles of the IL-4R.alpha. have been identified that have been variably assocd. with increased incidence of allergic disease, but there is little direct evidence that any variant is sufficient to alter a target that dets. allergic pathophysiol. or susceptibility. Variants of IL-4R.alpha. encoding isoleucine instead of valine at position 50 (I50 vs V50, resp.) can signal increased Stat6-dependent transcriptional activity, whether in an I50, Q551 or I50, R551 haplotype. Strikingly, signaling through these receptors did not increase the efficiency of Th2 development or the IL-4 mediated repression of Th1 development or a target gene, IL-18R.alpha.. Further, IL-4-induced proliferation was similar for Th2 cells independent of the variant expressed. Together these findings indicate that IL-4R.alpha. variants that exhibit gain-of-function with respect to Stat6 do not act directly through alterations in Th2/Th1 induction after Ag exposure. The data further suggest that for such variants, any mechanistic involvement is based on a role in cellular targets of Th2 cytokines.

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2  
AN 2004:97160 CAPLUS  
DN 140:180089  
TI NF-.kappa.B Controls Cell Fate Specification, Survival, and Molecular Differentiation of Immunoregulatory Natural T Lymphocytes  
AU Stanic, Aleksandar K.; Bezbradica, Jelena S.; Park, Jang-June; Matsuki, Naoto; \*\*\*Mora, Ana L.\*\*\* ; Van Kaer, Luc; Boothby, Mark R.; Joyce, Sebastian  
CS Department of Microbiology and Immunology, Vanderbilt University School of Medicine, Nashville, TN, 37232, USA  
SO Journal of Immunology (2004), 172(4), 2265-2273  
CODEN: JOIMA3; ISSN: 0022-1767  
PB American Association of Immunologists  
DT Journal  
LA English  
AB Ontogenetic, homeostatic, and functional deficiencies within immunoregulatory natural T (iNKT) lymphocytes underlie various

inflammatory immune disorders including autoimmunity. Signaling events that control cell fate specification and mol. differentiation of iNKT cells are only partly understood. Here we demonstrate that these processes within iNKT cells require classical NF-.kappa.B signaling. Inhibition of NF-.kappa.B signaling blocks iNKT cell ontogeny at an immature stage and reveals an apparent, novel precursor in which neg. selection occurs. Most importantly, this block occurs due to a lack of survival signals, as Bcl-xL overexpression rescues iNKT cell ontogeny. Maturation of immature iNKT cell precursors induces Bcl-2 expression, which is defective in the absence of NF-.kappa.B signaling. Bcl-xL overexpression also rescues this maturation-induced Bcl-2 expression. Thus, antiapoptotic signals relayed by NF-.kappa.B critically control cell fate specification and mol. differentiation of iNKT cells and, hence, reveal a novel role for such signals within the immune system.

RE.CNT 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3  
AN 2004:1044021 CAPLUS  
TI Susceptibility to allergic lung disease regulated by recall responses of dual-receptor memory T cells\*  
AU Aronica, Mark A.; Swaidani, Shadi; Zhang, Yan H.; Mitchell, Daphne;  
    \*\*\*Mora, Ana L.\*\*\* ; McCarthy, Susan; O'Neal, Jamye; Topham, David;  
Sheller, James R.; Boothby, Mark  
CS From the Department of Pulmonary, Allergy and Critical Care Medicine  
SO Journal of Allergy and Clinical Immunology (2004), 114(6), 1441-1448  
CODEN: JACIBY; ISSN: 0091-6749  
PB Elsevier Inc.  
DT Journal  
LA English  
AB Microbial infections are assocd. with the initial susceptibility to and flares of asthma. However, immunol. mechanisms whereby infections might alter the asthmatic phenotype are lacking. To test the hypothesis that memory T cells specific both for a viral antigen and an allergen could influence the pathogenesis of allergic disease *in vivo*. We developed a system in which 2 distinct T-cell receptors coexist on the T-cell surface, 1 specific for a virus and the other for an inhaled antigen. We show that a population of dual-receptor T cells, polarized through a virus-specific T-cell receptor to contain TH1 or TH2 cells, can be reactivated through an unrelated T-cell receptor in recall responses *in vivo*. Quiescent memory cells derived from a TH1-polarized effector population blocked the development of airway hyperreactivity in a model of allergic lung disease, in assocn. with decreased induction of chemokines and eosinophil recruitment. Conversely, reactivation of quiescent TH2 cells after inhalation of antigen or virus infection was sufficient to lead to the development of airway hyperresponsiveness and allergic pulmonary inflammation in mice whose lungs were previously normal. These data provide evidence that dual-receptor memory T cells can regulate allergic disease susceptibility and suggest that they may play a role in mediating the influence of microbes on asthma pathogenesis.

L4 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4  
AN 2003:601490 CAPLUS  
DN 139:196014  
TI New Programming of IL-4 Receptor Signal Transduction in Activated T Cells: Stat6 Induction and Th2 Differentiation Mediated by IL-4R. $\alpha$ . Lacking Cytoplasmic Tyrosines  
AU \*\*\*Mora, Ana L.\*\*\* ; Stephenson, Linda M.; Enerson, Ben; Youn, Jeehee;  
Keegan, Achsah D.; Boothby, Mark  
CS Dep. Microbiol., Vanderbilt Univ. Med. Sch., Nashville, TN, 37232, USA  
SO Journal of Immunology (2003), 171(4), 1891-1900  
CODEN: JOIMA3; ISSN: 0022-1767  
PB American Association of Immunologists  
DT Journal  
LA English  
AB Signaling by the IL-4 receptor . $\alpha$ -chain (IL-4R. $\alpha$ ) is a key determinant of the development of the Th2 lineage of effector T cells. Studies performed in tissue culture cell lines have indicated that tyrosines of the IL-4R. $\alpha$ . cytoplasmic tail are necessary for the induction of Stat6, a transcription factor required for Th2 differentiation. Surprisingly, we have found that in activated T cells,

IL-4R. $\alpha$  chains lacking all cytoplasmic tyrosines promote induction of this IL-4-specific transcription factor and efficient commitment to the Th2 lineage. Mutagenesis of a tyrosine-free cytoplasmic tail identifies a requirement for the serine-rich ID-1 region in this new program of IL-4R signal transduction obsd. in activated T cells. Addnl. findings suggest that an extracellular signal-regulated kinase pathway can be necessary and sufficient for the ability of such tyrosine-free IL-4R. $\alpha$  chains to mediate Stat6 induction. These results provide novel evidence that the mol. mechanisms by which a cytokine specifically induces a Stat transcription factor can depend on the activation state of T lymphoid cells. Furthermore, the data suggest that one pathway by which such new programming may be achieved is mediated by extracellular signal-regulated mitogen-activated protein kinases.

RE.CNT 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 5  
AN 2003:601470 CAPLUS  
DN 139:196206  
TI T Cell-Intrinsic Requirement for NF- $\kappa$ B Induction in Postdifferentiation IFN- $\gamma$ . Production and Clonal Expansion in a Th1 Response  
AU Corn, Radiah A.; Aronica, Mark A.; Zhang, Fuping; Tong, Yingkai; Stanley, Sarah A.; Kim, Se Ryoung Agnes; Stephenson, Linda; Enerson, Ben; McCarthy, Susan; \*\*\*Mora, Ana\*\*\* ; Boothby, Mark  
CS Department of Microbiology and Immunology, Vanderbilt University Medical School, Nashville, TN, 37232, USA  
SO Journal of Immunology (2003), 171(4), 1816-1824  
CODEN: JOIMA3; ISSN: 0022-1767  
PB American Association of Immunologists  
DT Journal  
LA English  
AB NF- $\kappa$ B/Rel transcription factors are linked to innate immune responses and APC activation. Whether and how the induction of NF- $\kappa$ B signaling in normal CD4+ T cells regulates effector function are not well-understood. The liberation of NF- $\kappa$ B dimers from inhibitors of  $\kappa$ B (I. $\kappa$ Bs) constitutes a central checkpoint for physiol. regulation of most forms of NF- $\kappa$ B. To investigate the role of NF- $\kappa$ B induction in effector T cell responses, we targeted inhibition of the NF- $\kappa$ B/Rel pathway specifically to T cells. The Th1 response *in vivo* is dramatically weakened when T cells defective in their NF- $\kappa$ B induction (referred to as I. $\kappa$ B. $\alpha$ (.DELTA.N) transgenic cells) are activated by a normal APC population. Analyses *in vivo*, and IL-12-supplemented T cell cultures *in vitro*, reveal that the mechanism underlying this T cell-intrinsic requirement for NF- $\kappa$ B involves activation of the IFN- $\gamma$ . gene in addn. to clonal expansion efficiency. The role of NF- $\kappa$ B in IFN- $\gamma$ . gene expression includes a modest decrease in Stat4 activation, T box expressed in T cell levels, and differentiation efficiency along with a more prominent postdifferentiation step. Further, induced expression of Bcl-3, a trans-activating I. $\kappa$ B-like protein, is decreased in T cells as a consequence of NF- $\kappa$ B inhibition. These findings indicate that NF- $\kappa$ B induction in T cells regulates efficient clonal expansion, Th1 differentiation, and IFN- $\gamma$ . prodn. by Th1 lymphocytes at a control point downstream from differentiation.

RE.CNT 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 6  
AN 2002:444995 CAPLUS  
DN 137:246465  
TI  $\beta$ .1 Integrin triggering affects leukemic cell line sensitivity to natural killer cells  
AU Rubio, Gonzalo; Ferez, Xabier; \*\*\*Mora, Ana\*\*\* ; Galvez, Jesus; Chicano, Antonio; Garcia-Penarrubia, Pilar  
CS Division of Immunology, Miguel Hernandez University, San Juan de Alicante, 03550, Spain  
SO Cancer Immunology Immunotherapy (2002), 51(3), 130-138  
CODEN: CIIMDN; ISSN: 0340-7004  
PB Springer-Verlag  
DT Journal

LA English  
AB The role of .beta.1 (CD29) integrins in natural killer (NK) cell-target cell conjugation and cytotoxicity has not been clearly established. Ligation of .beta.1 integrins in NK cells can modulate the lytic capacity in both a pos. and a neg. manner; however, the contribution of the .beta.1 integrins present on target cells remains to be evaluated. Here, we analyzed the effect of .beta.1 integrins expressed by potential tumor target cells on conjugation and cytotoxicity. Using normalized flow cytometry binding assays, we demonstrated that the pretreatment of MOLT-4, K562, U-937 and HL-60 human leukemia target cell lines with selected anti-.beta.1 monoclonal antibodies (mAb) increased conjugation to human NK cell line NKL as well as to purified NK cells. Only mAb recognizing residues 207-218 of the .beta.1 subunit and functionally involved in the induction of homotypic adhesion (functional epitope A1) increased conjugation of all the target cells. Moreover, mAb to adhesion mols. different from .beta.1 but also inducers of homotypic adhesion of the target cells, i.e. CD43 and CD50 (ICAM-3), failed to increase conjugation to NKL cells. Cytotoxicity assays demonstrated that lysis of NK-sensitive target cells (MOLT-4) also increased after pretreatment with anti-.beta.1 epitope A1 mAb. Importantly, pretreatment of NK-resistant target cells (U-937 and HL-60) with anti-.beta.1 mAb was not able to outweigh the cytotoxic inhibitory mechanisms controlled by HLA class I mols. However, simultaneous masking of HLA class I mols. with mAb and pretreatment with anti-.beta.1 mAb rendered NK-resistant cells susceptible to lysis, as predicted by the missing self hypothesis. Triggering of tumor target cells through .beta.1 integrins may thus play a role in conjugation to NK cells as well as in co-stimulation of cell-mediated cytotoxicity.

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2001:832559 CAPLUS  
DN 136:117323  
TI Inefficient ZAP-70 phosphorylation and decreased thymic selection in vivo result from inhibition of NF-.kappa.B/Rel  
AU \*\*\*Mora, Ana L.\*\*\* ; Stanley, Sarah; Armistead, Wade; Chan, Andrew C.; Boothby, Mark  
CS Department of Microbiology and Immunology, Vanderbilt University Medical School, Nashville, TN, 37232, USA  
SO Journal of Immunology (2001), 167(10), 5628-5635  
CODEN: JOIMA3; ISSN: 0022-1767  
PB American Association of Immunologists  
DT Journal  
LA English  
AB Signaling from the TCR regulates T lymphoid survival, deletion by apoptosis, and selective clonal expansion. One set of signaling pathways activated during thymic selection leads to degrdn. of a cytosolic retention protein, the inhibitor of .kappa.B (I.kappa.B).alpha., followed by nuclear translocation of the NF-.kappa.B/Rel family of transcription factors. It has been found previously that NF-.kappa.B proteins mediate a pathway signaling the survival of mature T cells and protection of thymocytes against TNF-induced apoptosis. In contrast, we show in this study that a transgenic inhibitor of NF-.kappa.B/Rel signaling interferes with the neg. selection of immature thymocytes by endogenous MHC ligands in vivo. Pos. selection of the H-Y TCR also was diminished. This attenuation of thymic selection efficiency was assocd. with decreased ZAP-70 phosphorylation and TCR signaling of CD69 induction. These findings demonstrate that the NF-.kappa.B transcriptional pathway plays an important role in normal processes of clonal deletion and they indicate that the NF-.kappa.B/I.kappa.B axis can regulate the efficiency of TCR signaling.

RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2001:125151 CAPLUS  
DN 134:294293  
TI NF-.kappa.B/rel participation in the lymphokine-dependent proliferation of T lymphoid cells  
AU \*\*\*Mora, Ana L.\*\*\* ; Youn, Jeehee; Keegan, Achsah D.; Boothby, Mark  
CS Department of Microbiology and Immunology, Vanderbilt University Medical

AN 2002:493395 CAPLUS  
DN 137:261439  
TI Lymphokine-dependent proliferation of T-lymphoid cells: regulated responsiveness and role in vivo  
AU Boothby, Mark; \*\*\*Mora, Ana L.\*\*\* ; Stephenson, Linda M.  
CS Department of Microbiology and Immunology, Vanderbilt University Medical School, Nashville, TN, 37232-2363, USA  
SO Critical Reviews in Immunology (2001), 21(6), 487-522  
CODEN: CCRIDE; ISSN: 1040-8401  
PB Begell House, Inc.  
DT Journal; General Review  
LA English  
AB A review. The discovery of lymphokines stemmed from their ability to promote T-lymphocyte proliferation in vitro. Even after 20 yr of intensive investigation, crucial aspects remain to be clarified about the role of specific lymphokines in T-cell proliferation and the biochemical mechanisms by which they play these roles, particularly in vivo. The present review focuses on conventional populations of TCR $\alpha$ .. $\beta$ . T cells. Older findings and new insights into the function of specific lymphokines in T-lymphocyte proliferation in vivo are summarized along with unanswered questions raised by these observations. Contributions of lymphokines to clonal proliferation arise from 2 processes: the protection of cells against apoptosis and the activation of cell cycling. Findings are underscored indicating that the activity of a particular lymphokine depends on the subset of T cells (CD4 vs. CD8; naive vs. memory) to which it binds, and that point to potential pitfalls of extrapolating from tissue culture-adapted models to the regulation of T cells in vivo. After summaries of signaling mechanisms related to the proliferative activity of lymphokines, recent findings are highlighted suggesting that such signaling is a regulated and plastic process rather than one fixed schema of action.

RE.CNT 267 THERE ARE 267 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2001:511936 CAPLUS  
DN 136:165511  
TI IL-4 signaling, gene transcription regulation, and the control of effector T cells  
AU Boothby, Mark; \*\*\*Mora, Ana L.\*\*\* ; Aronica, Mark A.; Youn, Jeehee; Sheller, James R.; Goenka, Shreevrat; Stephenson, Linda  
CS Department of Microbiology and Immunology and Medicine, Vanderbilt University Medical School, Nashville, TN, 37232-2363, USA  
SO Immunologic Research (2001), 23(2 & 3), 179-191  
CODEN: IMRSEB; ISSN: 0257-277X  
PB Humana Press Inc.  
DT Journal; General Review  
LA English  
AB A review. The central goal of the authors' research is to understand the regulation of lymphoid cells through molecular mechanisms of signal transduction and transcriptional control. A long-standing focus has been on changes that influence the effector function of mature lymphocytes. Work in the lab. is oriented toward the identification of new regulatory mechanisms using cell lines and primary cells, and the validation of these in vitro findings in mouse models of immune responses and diseases. Here, the authors summarize key insights into the regulation of T helper cell function during the phase of immunity where effector responses arise de novo. Particular interest has been centered on cytokine gene regulation as part of T cell differentiation into the Th1 and Th2 subsets. Information on IL-4 receptor signaling and the role of NF- $\kappa$ B transcription factors is reviewed. The authors' more recent work is designed to understand how regulation at the Th1/2 effector stages is related to the control of memory T cell survival, immune recall responses, and the role of these responses in immune-mediated disease.

RE.CNT 82 THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1999:329658 CAPLUS  
DN 131:115269  
TI Costimulation reverses the defect in IL-2 but not effector cytokine

AU production by T cells with impaired I.kappa.B.alpha. degradation  
Aune, Thomas M.; \*\*\*Mora, Ana L.\*\*\* ; Kim, Somee; Boothby, Mark;  
Lichtman, Andrew H.  
CS Department of Medicine (Rheumatology), Vanderbilt University Medical  
School, Nashville, TN, 37232, USA  
SO Journal of Immunology (1999), 162(10), 5805-5812  
CODEN: JOIMA3; ISSN: 0022-1767  
PB American Association of Immunologists  
DT Journal  
LA English  
AB Although the transcriptional basis for states of unresponsiveness in primary T cells is unclear, tolerant B lymphocytes exhibit inhibition of both c-Jun N-terminal kinase induction and I.kappa.B.alpha. (inhibitor of NF-.kappa.B.alpha.) degrdn., leading to lower levels of both nuclear AP-1 and NF-.kappa.B. Expression of an I.kappa.B.alpha. mutant resistant to signal-induced degrdn. in transgenic T cells caused markedly deficient effector cytokine (IL-4, IFN-.gamma.) prodn. after primary TCR stimulation despite a detectable level of nuclear NF-.kappa.B. A TCR response element from the IFN-.gamma. promoter, despite lacking detectable NF-.kappa.B/Rel sites, was also unresponsive to TCR ligation. Nuclear induction of AP-1 proteins in response to T cell activation was diminished in transgenic T cells. Costimulation induced by anti-CD28 mAb increased IL-2 prodn., but failed to reverse the defects in effector cytokine prodn. Taken together, these data indicate that impaired NF-.kappa.B/Rel signaling in T cells interferes with the signal transduction pathways required for efficient induction of effector cytokine prodn.

RE.CNT 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1999:692086 CAPLUS  
DN 132:34706  
TI Preferential role for NF-.kappa.B/Rel signaling in the type 1 but not type 2 T cell-dependent immune response in vivo  
AU Aronica, Mark A.; \*\*\*Mora, Ana L.\*\*\* ; Mitchell, Daphne B.; Finn, Patricia W.; Johnson, Joyce E.; Sheller, James R.; Boothby, Mark R.  
CS Divisions of Allergy, Pulmonary, Vanderbilt University Medical School, Nashville, TN, 37232, USA  
SO Journal of Immunology (1999), 163(9), 5116-5124  
CODEN: JOIMA3; ISSN: 0022-1767  
PB American Association of Immunologists  
DT Journal  
LA English  
AB T cell function is a crit. determinant of immune responses as well as susceptibility to allergic diseases. Activated T cells can differentiate into effectors whose cytokine profile is limited to type 1 (IFN-.gamma.-dominant) or type 2 (IL-4-, IL-5-dominant) patterns. To investigate mechanisms that connect extracellular stimuli with the regulation of effector T cell function, we have measured immune responses of transgenic mice whose NF-.kappa.B/Rel signaling pathway is inhibited in T cells. Surprisingly, these mice developed type 2 T cell-dependent responses (IgE and eosinophil recruitment) in a model of allergic pulmonary inflammation. In contrast, type 1 T cell responses were severely impaired, as evidenced by markedly diminished delayed-type hypersensitivity responses, IFN-.gamma. prodn., and Ag-specific IgG2a levels. Taken together, these data indicate that inhibition of NF-.kappa.B can lead to preferential impairment of type 1 as compared with type 2 T cell-dependent responses.

RE.CNT 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1999:597980 CAPLUS  
DN 131:227644  
TI Lineage-specific differences among CD8+ T cells in their dependence of NF-.vkappa.B/Rel signaling  
AU \*\*\*Mora, Ana L.\*\*\* ; Chen, Daohong; Boothby, Mark; Rubin, Donald H.  
CS Dep. Microbiology Immunology, Medical School, Vanderbilt Univ., Nashville, TN, 37232, USA  
SO European Journal of Immunology (1999), 29(9), 2968-2980  
CODEN: EJIMAF; ISSN: 0014-2980

PB Wiley-VCH Verlag GmbH  
DT Journal  
LA English  
AB Whereas most CD8+ T cells in lymph nodes and spleen express the CD8.alpha..beta. heterodimer and depend absolutely on thymic competence for their development, a substantial population of T cells expressing CD8.alpha..alpha. matures extrathymically. Although the existence of these CD8 sublineages is well established, relatively little is known about differences that might exist among CD8 cells in their requirement for particular transcriptional pathways during the development and maintenance of normal populations. Transgenic mice whose T lineage expresses an I.vkappa.B.alpha. mutant exhibited decreased NF-.vkappa.B signaling and a diminution in mature CD8 T cells. The authors detd. that although TCR-dependent CD69 induction by CD8.alpha..alpha. and CD8.alpha..beta. T cells was unaffected by inhibition of NF-.vkappa.B, TCR.alpha..beta. CD8.alpha..beta. T cells were preferentially reduced compared to their TCR.alpha..beta. CD8.alpha..alpha. or TCR.gamma..delta. counterparts. This finding was most prominent in spleen, but was also apparent in Peyer's patches of transgenic mice. Diminished antiviral cytotoxic responses of CD8.alpha..beta. intraepithelial lymphocytes were obsd. after enteric reovirus infection. These results indicate that NF-.vkappa.B signaling is more important for the thymus-dependent TCR.alpha..beta. CD8.alpha..beta. population than for other CD8 lineages, and thus regulates the no., function, and normal balance of CD8 subsets in the periphery.

RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1999:477330 CAPLUS  
DN 131:256215  
TI Essential role of T cell NF-.kappa.B activation in collagen-induced arthritis  
AU Seetharaman, Rajalakshmi; \*\*\*Mora, Ana L.\*\*\* ; Nabozny, Gerald;  
Boothby, Mark; Chen, Jin  
CS Departments of Medicine/Rheumatology and Cell Biology, Vanderbilt  
University, Nashville, TN, 37232, USA  
SO Journal of Immunology (1999), 163(3), 1577-1583  
CODEN: JOIMA3; ISSN: 0022-1767  
PB American Association of Immunologists  
DT Journal  
LA English  
AB NF-.kappa.B/Rel proteins are ubiquitous transcription factors that are activated by proinflammatory signals or engagement of antigen (Ag) receptors. To study the role of NF-.kappa.B/Rel signaling in T lymphocytes during autoimmune disease, the authors investigated type II collagen-induced arthritis (CIA) in transgenic mice expressing a constitutive inhibitor of NF-.kappa.B/Rel [I.kappa.B.alpha.(.DELTA.N)] in the T lineage. Expression of the I.kappa.B.alpha.(.DELTA.N) transgene was persistently high in adult peripheral lymphoid organs and undetectable in T cell-depleted splenocytes, suggesting the expression of the transgene is restricted to the T lineage. The incidence and severity of CIA were decreased in these I.kappa.B.alpha.(.DELTA.N) transgenic mice compared with non-transgenic littermates. Inhibition of CIA was not due solely to a decrease in their CD8+ population because transfer of wild-type CD8+ cells into transgenic mice failed to restore disease susceptibility. Protection against disease was assocd. with a moderate decrease in clonal expansion and a profound and persistent decrease in Ag-induced IFN-.gamma. prodn. in vivo. Consistent with decreased level of anti-type II collagen-specific Abs and IFN-.gamma., serum levels of IgG2a anti-CII Abs were reduced. However, anti-CII-specific IgG1 levels were normal, indicating that some aspects of T cell help were unaffected. Apparently, inhibition of NF-.kappa.B in T cells impairs CIA development in vivo through decreases in type 1 T cell-dependent responses.

RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1998:651707 CAPLUS  
DN 130:37000  
TI Controlled lipidation and encapsulation of peptides as a useful approach

to mucosal immunizations  
AU     \*\*\*Mora, Ana L.\*\*\* ; Tam, James P.  
CS     Dep. of Microbiology and Immunology, Vanderbilt University, Nashville, TN,  
      37232-2363, USA  
SO     Journal of Immunology (1998), 161(7), 3616-3623  
      CODEN: JOIMA3; ISSN: 0022-1767  
PB     American Association of Immunologists  
DT     Journal  
LA     English  
AB     To generate a useful strategy for mucosal immunization, we have developed  
      an approach of lipidating a multiple Ag peptide (mAP) contg. part of the  
      V3 loop from HIV-1 gp120IIIB. In this work, we compare two delivery  
      systems, lipidated MAP in PBS and encapsulation in poly(DL-lactide-co-  
      glycolide) microparticles. S.c. immunization, followed by intragastric  
      administration of MAP peptide entrapped or not entrapped in  
      microparticles, induced mucosal and systemic immune responses at local and  
      distant sites, including mucosal IgA in saliva, vaginal secretions and  
      feces, and IgG in blood. However, lipidated Ag delivered in  
      microparticles induced higher levels of mucosal Abs, particularly of  
      intestinal IgA, and generated CTL responses. In contrast, lipidated MAP  
      delivered by nasal route microparticles was less effective in inducing CTL  
      responses. These results demonstrate the feasibility of using a lipidated  
      multimeric peptide for mucosal immunization to stimulate both systemic and  
      mucosal immune systems, including the genital tract, irresp. of the route  
      or method of delivery and without requiring the use of a carrier or an  
      extraneous adjuvant.

RE.CNT 48    THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD  
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4     ANSWER 18 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN  
AN     1998:746694 CAPLUS  
DN     130:109125  
TI     In vivo function of an interleukin 2 receptor .beta. chain  
      (IL-2R.beta.)/IL-4R.alpha. cytokine receptor chimera potentiates allergic  
      airway disease  
AU     Youn, Jeehee; Chen, Jin; Goenka, Shreevrat; Aronica, Mark A.;    \*\*\*Mora,\*\*\*  
      \*\*\*    Ana L.\*\*\* ; Correa, Victor; Sheller, James R.; Boothby, Mark  
CS     Department of Microbiology and Immunology, Department of Medicine,  
      Vanderbilt University Medical School, Nashville, TN, 37232, USA  
SO     Journal of Experimental Medicine (1998), 188(10), 1803-1816  
      CODEN: JEMEAV; ISSN: 0022-1007  
PB     Rockefeller University Press  
DT     Journal  
LA     English  
AB     Strength of T cell receptor (TCR) signaling, coreceptors, costimulation,  
      antigen-presenting cell type, and cytokines all play crucial roles in  
      detg. the efficiency with which type 2 T lymphocytes (Th2, Tc2) develop  
      from uncommitted precursors. To investigate in vivo regulatory mechanisms  
      that control the population of type 2 T cells and disease susceptibility,  
      the authors have created lines of transgenic mice in which expression of a  
      chimeric cytokine receptor (the mouse interleukin 2 receptor .beta. chain  
      [IL-2R.beta.] extracellular domain fused to the cytoplasmic tail of  
      IL-4R.alpha.) is targeted to the T lymphoid lineage using the proximal lck  
      promoter. This chimera transduced IL-4-specific signals in response to  
      IL-2 binding and dramatically enhanced type 2 responses (IL-4, IL-5, and  
      IgE prodn.) upon in vitro TCR stimulation or in vivo antigen challenge.  
      Thus, type 2 effector function was augmented by IL-4 signals transduced  
      through a chimeric receptor expressed in a T cell-specific manner. This  
      influence was sufficient for establishment of antigen-induced allergic  
      airway hyperresponsiveness on a disease-resistant background (C57BL/6).

RE.CNT 80    THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD  
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4     ANSWER 19 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN  
AN     1998:652614 CAPLUS  
DN     130:13192  
TI     Stimulus-dependent synergism of the antiapoptotic tumor necrosis factor  
      receptor-associated factor 2 (TRAF2) and nuclear factor .kappa.B pathways  
AU     Lee, Soo Young; Kaufman, David R.;    \*\*\*Mora, Ana L.\*\*\* ; Santana,  
      Angela; Boothby, Mark; Choi, Yongwon  
CS     Department of Pathology, Hallym Medical School, Kangwon, 200-702, S. Korea

SO Journal of Experimental Medicine (1998), 188(7), 1381-1384  
CODEN: JEMEA; ISSN: 0022-1007  
PB Rockefeller University Press  
DT Journal  
LA English  
AB Tumor necrosis factor (TNF) signaling leads to pleiotropic responses in a wide range of cell types, in part by activating antiapoptotic and proapoptotic signaling pathways. Thus, although TNF can cause apoptosis and may prove useful in the treatment of malignancies, most cells are resistant to TNF-induced cell death unless *de novo* protein synthesis is inhibited. Previous studies suggested that TNF activation of the nuclear factor (NF)-.kappa.B transcription factor family antagonizes the proapoptotic signals initiated by TNF-.alpha.. TNF receptor-assocd. factor (TRAF)2 has also been shown to mediate crucial antiapoptotic signals during TNF stimulation, yet is not essential in activation of NF-.kappa.B under physiol. conditions, thus raising questions about the relation between these antiapoptotic pathways. The authors report here that inhibition of TRAF2 and NF-.kappa.B function in primary cells, by coexpression of a constitutive repressor of multiple NF-.kappa.B/Rel proteins (I.kappa.B.alpha..DN) and a dominant neg. form of TRAF2 (TRAF2.DN), synergistically enhanced TNF-induced apoptosis. The effects were stimulus dependent, such that neither inhibitory mol. affected Fas- and daunorubicin-induced apoptosis to the same degree as TNF-induced death. Thus, the NF-.kappa.B and TRAF2 pathways activate independent antiapoptotic mechanisms which act in concert to suppress the proapoptotic signals induced by TNF-.alpha..

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1997:359279 CAPLUS  
DN 127:94072  
TI Perturbation of the T lymphocyte lineage in transgenic mice expressing a constitutive repressor of nuclear factor (NF)-.kappa.B  
AU Boothby, Mark R.; \*\*\*Mora, Ana L.\*\*\* ; Scherer, David C.; Brockman, Jeffrey A.; Ballard, Dean W.  
CS Department of Microbiology and Immunology; rheumatology Division, Department of Medicine; and the Howard Hughes Medical Institute, Vanderbilt University Medical Center, Nashville, TN, 37232, USA  
SO Journal of Experimental Medicine (1997), 185(11), 1897-1907  
CODEN: JEMEA; ISSN: 0022-1007  
PB Rockefeller University Press  
DT Journal  
LA English  
AB Members of the nuclear factor (NF)-.kappa.B/Rel family transcription factors are induced during thymic selection and in mature T lymphocytes after ligation of the T cell antigen receptor (TCR). Despite these findings, disruption of individual NF-.kappa.B/Rel genes has revealed no intrinsic defect in the development of mature T cells, perhaps reflecting functional redundancy. To circumvent this possibility, the T cell lineage was targeted to express a trans-dominant form of I.kappa.B.alpha. that constitutively represses the activity of multiple NF-.kappa.B/Rel proteins. Transgenic cells expressing this inhibitor exhibit a significant proliferative defect, which is not reversed by the addn. of exogenous interleukin-2. Moreover, mitogenic stimulation of splenocytes leads to increased apoptosis of transgenic T cells as compared with controls. In addn. to deregulated T cell growth and survival, transgene expression impairs the development of normal T cell populations as evidenced by diminished nos. of TCRhi CD8 single-pos. thymocytes. This defect was significantly amplified in the periphery and was accompanied by a decrease in CD4+ T cells. Taken together, these *in vivo* findings indicate that the NF-.kappa.B/Rel signaling pathway contains compensatory components that are essential for the establishment of normal T cell subsets.

RE.CNT 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1992:4741 CAPLUS  
DN 116:4741  
TI Molecular analysis of HLA DR4-.beta.1 gene in malaria vaccinees. Typing

AU and subtyping by PCR technique and oligonucleotides  
Murillo, Luis Angel; Rocha, Claudia Lucia; \*\*\*Mora, Ana Lucia\*\*\* ;  
Kalil, Jorge; Goldenberg, Ana Karla; Patarroyo, Manuel Elkin  
CS Inst. Immunol., Hosp. San Juan de Dios, Bogota, Colombia  
SO Parasite Immunology (1991), 13(2), 201-10  
CODEN: PAIMD8; ISSN: 0141-9838  
DT Journal  
LA English  
AB The combination of the polymerase chain reaction (PCR) technique and synthetic oligonucleotides has proved to be a useful tool in the mol. anal. of HLA class II genes, allowing recognition of as little as a single nucleotide modification in the sequence of the gene. The mols. encoded by these genes have been assocd. with genetic control of the immune response and with susceptibility to certain diseases. Studies by the authors have shown 3 patterns of humoral immune response in the human volunteers vaccinated with the synthetic protein SPf 66; high, intermediate and low responders. Approx. 73.3% of the low responders were serol. typed as HLA DR4 and 42% as DQw6. These results encouraged a search for a subtype (Dw) correlation between the DR4 pos. individuals and the different humoral immune response patterns. Using oligotyping methods after previous amplification of the DR4 B1 exon, 20 DR4 volunteers were subtyped and classified as high, intermediate, and low responders. No direct assocn. was found between the HLA DR4 Dw special subtype in the high or low responders immunized with the SPf 66 vaccine.

=> s (fusion protein?) and (translocating) and IkappaB?  
6 FILES SEARCHED...  
L5 10 (FUSION PROTEIN?) AND (TRANSLOCATING) AND IKAPPAB?

=> dup rem 15  
PROCESSING COMPLETED FOR L5  
L6 10 DUP REM L5 (0 DUPLICATES REMOVED)

=> d bib ab 1-  
YOU HAVE REQUESTED DATA FROM 10 ANSWERS - CONTINUE? Y/(N):y

L6 ANSWER 1 OF 10 USPATFULL on STN  
AN 2004:306965 USPATFULL  
TI Monitoring gene silencing and annotating gene function in living cells  
IN Michnick, Stephen William Watson, Westmount, CANADA  
Belisle, Barbara, Moraga, CA, UNITED STATES  
MacDonald, Marnie L., Pleasanton, CA, UNITED STATES  
Westwick, John K., San Ramon, CA, UNITED STATES  
Lamerdin, Jane Elizabeth, Livermore, CA, UNITED STATES  
PI US 2004241636 A1 20041202  
AI US 2004-856620 A1 20040529 (10)  
PRAI US 2003-474283P 20030530 (60)  
DT Utility  
FS APPLICATION  
LREP Isaac A. Angres, Suite 301, 2001 Jefferson Davis Highway, Arlington, VA, 22202  
CLMN Number of Claims: 14  
ECL Exemplary Claim: 1  
DRWN .16 Drawing Page(s)  
LN.CNT 2073

CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB The cell-based assays described in the present invention can be used to directly assess the sensitivity and specificity of the gene annotation reagent against its target, and to determine if a non-targeted gene participates in a pathway of interest or is functionally linked to another gene or protein. The combination of annotation reagents with such cell-based assays is useful for mapping genes (proteins) into cellular pathways on a genome-wide scale. Preferred assay embodiments include fluorescence or luminescence assays in intact (live or fixed) cells. Such fluorescence or luminescence assays include high-throughput or high-content assays for protein activity, subcellular localization, post-translational modifications, or interactions of proteins. Suitable assays may include protein-protein interaction assays; protein translocation assays; and post-translational modification assays. The invention can be used to assess the efficacy of any gene silencing

experiment, to determine the level of gene silencing that is achieved, and to map novel genes into biochemical pathways, and to identify novel pharmaceutical targets. The results also demonstrate the feasibility of employing this strategy in genome-wide functional annotation efforts.

L6 ANSWER 2 OF 10 USPATFULL on STN  
AN 2004:298665 USPATFULL  
TI Peptides for use as translocation factors  
IN Crisanti, Andrea, London, UNITED KINGDOM  
PI US 2004234527 A1 20041125  
AI US 2004-479166 A1 20040429 (10)  
WO 2002-GB3027 20020701  
PRAI GB 2001-16047 20010629  
DT Utility  
FS APPLICATION  
LREP SALIWANCHIK LLOYD & SALIWANCHIK, A PROFESSIONAL ASSOCIATION, PO BOX 142950, GAINESVILLE, FL, 32614-2950  
CLMN Number of Claims: 39  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 1271  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB Proteins that contain the amino acid sequence motif X.sup.1X.sup.1X.sup.2X.sup.3X.sup.1, where X.sup.1=R or K and X.sup.2 and X.sup.3=any amino acid have been found to translocate and can therefore be used in the manufacture of compositions for therapeutic applications. The proteins may also be used as translocation factors to deliver proteins or nucleic acids into a cell.

L6 ANSWER 3 OF 10 USPATFULL on STN  
AN 2004:196424 USPATFULL  
TI Lectin compositions and methods for modulating an immune response to an antigen  
IN Segal, Andrew H., Boston, MA, UNITED STATES  
Young, Elihu, Sharon, MA, UNITED STATES  
PA Genitrix, LLC (U.S. corporation)  
PI US 2004151728 A1 20040805  
AI US 2003-666834 A1 20030919 (10)  
RLI Division of Ser. No. US 2003-645000, filed on 20 Aug 2003, PENDING  
PRAI US 2002-404823P 20020820 (60)  
US 2003-487407P 20030715 (60)  
DT Utility  
FS APPLICATION  
LREP PALMER & DODGE, LLP, KATHLEEN M. WILLIAMS, 111 HUNTINGTON AVENUE, BOSTON, MA, 02199  
CLMN Number of Claims: 77  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 39129  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB The present invention provides a fusion polypeptide which can bind to a cell surface binding moiety (e.g., a carbohydrate) and serve as a ligand for a cell surface polypeptide, as well as a vector comprising a nucleic acid encoding for such a fusion polypeptide, and a host cell comprising such nucleic acid. The present invention also provides a composition comprising an antigen bearing target and such a fusion polypeptide, as well as a composition comprising a virus or a cell and such a fusion polypeptide. The present invention further relates to a method of modulating an immune response in an animal using such compositions.

L6 ANSWER 4 OF 10 USPATFULL on STN  
AN 2004:165307 USPATFULL  
TI Lectin compositions and methods for modulating an immune response to an antigen  
IN Segal, Andrew H., Boston, MA, UNITED STATES  
Young, Elihu, Sharon, MA, UNITED STATES  
PA Genitrix, LLC (U.S. corporation)  
PI US 2004126793 A1 20040701  
AI US 2003-666885 A1 20030919 (10)  
RLI Division of Ser. No. US 2003-645000, filed on 20 Aug 2003, PENDING  
PRAI US 2002-404823P 20020820 (60)

US 2003-487407P 20030715 (60)  
DT Utility  
FS APPLICATION  
LREP PALMER & DODGE, LLP, KATHLEEN M. WILLIAMS, 111 HUNTINGTON AVENUE,  
BOSTON, MA, 02199  
CLMN Number of Claims: 147  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 28979

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a fusion polypeptide which can bind to a cell surface binding moiety (e.g., a carbohydrate) and serve as a ligand for a cell surface polypeptide, as well as a vector comprising a nucleic acid encoding for such a fusion polypeptide, and a host cell comprising such nucleic acid. The present invention also provides a composition comprising an antigen bearing target and such a fusion polypeptide, as well as a composition comprising a virus or a cell and such a fusion polypeptide. The present invention further relates to a method of modulating an immune response in an animal using such compositions.

L6 ANSWER 5 OF 10 USPATFULL on STN  
AN 2004:164872 USPATFULL  
TI Lectin compositions and methods for modulating an immune response to an antigen  
IN Segal, Andrew H., Boston, MA, UNITED STATES  
Young, Elihu, Sharon, MA, UNITED STATES  
PA Genitrix, LLC (U.S. corporation)  
PI US 2004126357 A1 20040701  
AI US 2003-666886 A1 20030919 (10)  
RLI Division of Ser. No. US 2003-645000, filed on 20 Aug 2003, PENDING  
PRAI US 2002-404823P 20020820 (60)  
US 2003-487407P 20030715 (60)  
DT Utility  
FS APPLICATION  
LREP PALMER & DODGE, LLP, KATHLEEN M. WILLIAMS, 111 HUNTINGTON AVENUE,  
BOSTON, MA, 02199  
CLMN Number of Claims: 11  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 39007

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a fusion polypeptide which can bind to a cell surface binding moiety (e.g., a carbohydrate) and serve as a ligand for a cell surface polypeptide, as well as a vector comprising a nucleic acid encoding for such a fusion polypeptide, and a host cell comprising such nucleic acid. The present invention also provides a composition comprising an antigen bearing target and such a fusion polypeptide, as well as a composition comprising a virus or a cell and such a fusion polypeptide. The present invention further relates to a method of modulating an immune response in an animal using such compositions.

L6 ANSWER 6 OF 10 USPATFULL on STN  
AN 2004:12959 USPATFULL  
TI Methods and compositions for diagnosing or monitoring auto immune and chronic inflammatory diseases  
IN Wohlgemuth, Jay, Palo Alto, CA, UNITED STATES  
Fry, Kirk, Palo Alto, CA, UNITED STATES  
Woodward, Robert, Pleasanton, CA, UNITED STATES  
Ly, Ngoc, San Bruno, CA, UNITED STATES  
PI US 2004009479 A1 20040115  
AI US 2002-131827 A1 20020424 (10)  
RLI Continuation-in-part of Ser. No. US 2001-6290, filed on 22 Oct 2001,  
PENDING  
PRAI US 2001-296764P 20010608 (60)  
DT Utility  
FS APPLICATION  
LREP Michael R. Ward, Morrison & Foerster LLP, 425 Market Street, San  
Francisco, CA, 94105-2482  
CLMN Number of Claims: 19  
ECL Exemplary Claim: 1  
DRWN 12 Drawing Page(s)

LN.CNT 19677

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods of diagnosing or monitoring an autoimmune or chronic inflammatory disease, particularly SLE in a patient by detecting the expression level of one or more genes or surrogates derived therefrom in the patient are described. Diagnostic oligonucleotides for diagnosing or monitoring chronic inflammatory disease, particularly SLE infection and kits or systems containing the same are also described.

L6 ANSWER 7 OF 10 USPATFULL on STN

AN 2003:220740 USPATFULL

TI Methods and compositions for diagnosing and treating rheumatoid arthritis

IN Pittman, Debra D., Windham, NH, UNITED STATES  
Feldman, Jeffrey L., Arlington, MA, UNITED STATES  
Shields, Kathleen M., Harvard, MA, UNITED STATES  
Trepicchio, William L., Andover, MA, UNITED STATES

PI US 2003154032 A1 20030814

AI US 2001-23451 A1 20011217 (10)

PRAI US 2000-255861P 20001215 (60)

DT Utility

FS APPLICATION

LREP Patent Group, FOLEY, HOAG & ELIOT LLP, One Post Office Square, Boston, MA, 02109

CLMN Number of Claims: 40

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 25385

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides methods and compositions for diagnostic assays for detecting R.A. and therapeutic methods and compositions for treating R.A. The invention also provides methods for designing, identifying, and optimizing therapeutics for R.A. Diagnostic compositions of the invention include compositions comprising detection agents for detecting one or more genes that have been shown to be up- or down-regulated in cells of R.A. relative to normal counterpart cells. Exemplary detection agents include nucleic acid probes, which can be in solution or attached to a solid surface, e.g., in the form of a microarray. The invention also provides computer-readable media comprising values of levels of expression of one or more genes that are up- or down-regulated in R.A.

L6 ANSWER 8 OF 10 USPATFULL on STN

AN 2003:99724 USPATFULL

TI Proteins and druggable regions of proteins

IN Edwards, Aled, Toronto, CANADA

Arrowsmith, Cheryl, North York, CANADA

Greenblatt, Jack, Toronto, CANADA

Mendlein, John D., Encinitas, CA, UNITED STATES

PI US 2003068831 A1 20030410

AI US 2002-97125 A1 20020312 (10)

PRAI US 2001-275216P 20010312 (60)

DT Utility

FS APPLICATION

LREP FOLEY HOAG LLP, PATENT GROUP, WORLD TRADE CENTER WEST, 155 SEAPORT BOULEVARD, BOSTON, MA, 02110-2600

CLMN Number of Claims: 31

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 4944

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to methods for learning structural information about a molecule or molecular complex. The invention also provides methods for identifying a compound that binds to a molecule or molecular complex. The invention also provides methods for identifying a compound that binds to one molecule or molecular complex and not to one or more other molecules or molecular complexes. Other methods that are provided can be used to identify a compound that binds to at least two molecules or molecular complexes.

L6 ANSWER 9 OF 10 USPATFULL on STN

AN 2003:99546 USPATFULL

TI Multi-target analysis of gene families for chemistry of high affinity and selective small molecules and other therapeutics

IN Arrowsmith, Cheryl, North York, CANADA

Greenblatt, Jack, Toronto, CANADA

Edwards, Aled, Toronto, CANADA

Mendlein, John D., Encincitas, CA, UNITED STATES

PI US 2003068651 A1 20030410

AI US 2002-97194 A1 20020312 (10)

PRAI US 2001-275216P 20010312 (60)

DT Utility

FS APPLICATION

LREP FOLEY HOAG LLP, PATENT GROUP, WORLD TRADE CENTER WEST, 155 SEAPORT BOULEVARD, BOSTON, MA, 02110-2600

CLMN Number of Claims: 79

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 5161

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to methods for learning structural information about a molecule or molecular complex. The invention also provides methods for identifying a compound that binds to a molecule or molecular complex. The invention also provides methods for identifying a compound that binds to one molecule or molecular complex and not to one or more other molecules or molecular complexes. Other methods that are provided can be used to identify a compound that binds to at least two molecules or molecular complexes.

L6 ANSWER 10 OF 10 USPATFULL on STN

AN 2003:99545 USPATFULL

TI Target analysis for chemistry of specific and broad spectrum anti-infectives and other therapeutics

IN Greenblatt, Jack, Toronto, CANADA

Edwards, Aled, Toronto, CANADA

Arrowsmith, Cheryl, North York, CANADA

Mendlein, John D., Encincitas, CA, UNITED STATES

PI US 2003068650 A1 20030410

AI US 2002-97193 A1 20020312 (10)

PRAI US 2001-275216P 20010312 (60)

DT Utility

FS APPLICATION

LREP FOLEY HOAG LLP, PATENT GROUP, WORLD TRADE CENTER WEST, 155 SEAPORT BOULEVARD, BOSTON, MA, 02110-2600

CLMN Number of Claims: 52

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 5051

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to methods for learning structural information about a molecule or molecular complex. The invention also provides methods for identifying a compound that binds to a molecule or molecular complex. The invention also provides methods for identifying a compound that binds to one molecule or molecular complex and not to one or more other molecules or molecular complexes. Other methods that are provided can be used to identify a compound that binds to at least two molecules or molecular complexes.

=> d bib ab kwic 10

L6 ANSWER 10 OF 10 USPATFULL on STN

AN 2003:99545 USPATFULL

TI Target analysis for chemistry of specific and broad spectrum anti-infectives and other therapeutics

IN Greenblatt, Jack, Toronto, CANADA

Edwards, Aled, Toronto, CANADA

Arrowsmith, Cheryl, North York, CANADA

Mendlein, John D., Encincitas, CA, UNITED STATES

PI US 2003068650 A1 20030410

AI US 2002-97193 A1 20020312 (10)

PRAI US 2001-275216P 20010312 (60)

DT Utility

FS APPLICATION

LREP FOLEY HOAG LLP, PATENT GROUP, WORLD TRADE CENTER WEST, 155 SEAPORT BOULEVARD, BOSTON, MA, 02110-2600

CLMN Number of Claims: 52

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 5051

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to methods for learning structural information about a molecule or molecular complex. The invention also provides methods for identifying a compound that binds to a molecule or molecular complex. The invention also provides methods for identifying a compound that binds to one molecule or molecular complex and not to one or more other molecules or molecular complexes. Other methods that are provided can be used to identify a compound that binds to at least two molecules or molecular complexes.

SUMM [0049] A " \*\*\*fusion\*\*\* \*\*\*protein\*\*\* " or "fusion polypeptide" refers to a polypeptide comprising a first amino acid sequence encoding a polypeptide linked to at least. . . not substantially homologous with any domain of the first polypeptide. The two polypeptide sequences may be linked in frame. A \*\*\*fusion\*\*\* \*\*\*protein\*\*\* may include a domain which is found (albeit in a different protein) in an organism which also expresses the first. . . fusion polypeptides may be fused to the N-terminus, the C-terminus, or the N- and C-terminus of the first polypeptide. Exemplary \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* include polypeptides comprising a glutathione S-transferase tag (GST-tag), histidine tag (His-tag), an immunoglobulin domain or an immunoglobulin binding domain.

SUMM . . . synthesizer or by recombinant techniques or combinations thereof), a recombinant test compound, a natural or a non-natural test compound, a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* or equivalent thereof and mutants, derivatives or combinations thereof.

SUMM [0135] In certain embodiments, a polypeptide which may be used in accordance with the methods of the invention is a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* containing a domain which increases its solubility and/or facilitates its purification, identification, detection, and/or structural or functional characterization. Exemplary domains, . . . protein A, protein G, calmodulin-binding peptide, thioredoxin, maltose binding protein, HA, myc, poly arginine, poly His, poly His-Asp or FLAG \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* and tags. Additional exemplary domains include domains that alter protein localization in vivo, such as signal peptides, type III secretion. . . the invention to include linker sequences between the polypeptide and the fusion domain in order to facilitate construction of the \*\*\*fusion\*\*\* \*\*\*protein\*\*\* or to optimize protein expression or structural constraints of the \*\*\*fusion\*\*\* \*\*\*protein\*\*\*. In another embodiment, the polypeptide may be constructed so as to contain protease cleavage sites between the fusion polypeptide and. . .

SUMM . . . Chem 269:10444-10450; and Perez et al. (1992) J Cell Sci 102:717-722). The transcytosis polypeptide may also be a non-naturally occurring membrane- \*\*\*translocating\*\*\* sequence (MTS), such as the peptide sequences disclosed in U.S. Pat. No. 6,248,558.

SUMM . . . of the invention may be tested for binding activity, as well as inhibitory ability, by expression as, for example, thioredoxin \*\*\*fusion\*\*\* \*\*\*proteins\*\*\*, each of which contains a discrete fragment of a protein of the invention (see, for example, U.S. Pat. Nos. 5,270,181. . .

SUMM . . . that the degenerate set of potential nucleotide sequences are expressible as individual polypeptides, or alternatively, as a set of larger \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* (e.g. for phage display).

SUMM . . . et al., WO 88/06630; Fuchs et al., (1991) Bio/Technology 9:1370-1371; and Goward et al., (1992) TIBS 18:136-140), and the resulting \*\*\*fusion\*\*\* \*\*\*protein\*\*\* detected by panning, e.g. using a fluorescently labeled molecule which binds the cell surface protein, e.g. FITC-substrate, to score for. . .

SUMM [0157] In similar fashion, the gene library may be expressed as a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* on the surface of a viral particle. For instance, in the filamentous phage system, foreign peptide sequences may be expressed. . . used in phage display libraries, as either of the phage gIII or gVIII coat proteins may be used to generate \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* without disrupting the ultimate packaging of the viral

particle (Ladner et al., PCT publication WO 90/02909; Garrard et al., PCT. . . .  
SUMM . . . construct which includes coding sequences for a late vaccinia virus structural protein to produce a set of recombinant viruses expressing \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* comprising a portion of the protein as part of the virion. The Hepatitis B surface antigen may also be utilized in this role as well. Similarly, chimeric constructs coding for \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* containing a portion of a polypeptide and the poliovirus capsid protein may be created to enhance immunogenicity (see, for example, . . . .  
SUMM . . . cleavage site sequence at the N-terminus of the desired portion of the recombinant protein, may allow purification of the expressed \*\*\*fusion\*\*\* \*\*\*protein\*\*\* by affinity chromatography using a Ni.sup.2+ metal resin. The purification leader sequence may then be subsequently removed by treatment with. . . .  
DETD . . . GRK-7 AF282269  
receptor kinases  
(GRKs)  
Hexokinase cancer type II  
NM\_000189  
Casein Kinase  
Glycogen  
Synthase Kinase  
(GSK),  
LIM Kinase  
(actin-binding  
kinase  
\*\*\*IkappaB\*\*\*  
Kinases (IKK),  
Rock and Related  
Rho Interacting  
Proteins (protein  
kinases)  
Pyruvate  
Dehydrogenase  
Kinase (PDK)  
IL-1 receptor  
kinases  
Calcium/calmodu  
lin-dependent  
protein. . . .

=> d bib ab 9

L6 ANSWER 9 OF 10 USPATFULL on STN  
AN 2003:99546 USPATFULL  
TI Multi-target analysis of gene families for chemistry of high affinity and selective small molecules and other therapeutics  
IN Arrowsmith, Cheryl, North York, CANADA  
Greenblatt, Jack, Toronto, CANADA  
Edwards, Aled, Toronto, CANADA  
Mendlein, John D., Encinitas, CA, UNITED STATES  
PI US 2003068651 A1 20030410  
AI US 2002-97194 A1 20020312 (10)  
PRAI US 2001-275216P 20010312 (60)  
DT Utility  
FS APPLICATION  
LREP FOLEY HOAG LLP, PATENT GROUP, WORLD TRADE CENTER WEST, 155 SEAPORT BOULEVARD, BOSTON, MA, 02110-2600  
CLMN Number of Claims: 79  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 5161  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB The present invention relates to methods for learning structural information about a molecule or molecular complex. The invention also provides methods for identifying a compound that binds to a molecule or molecular complex. The invention also provides methods for identifying a compound that binds to one molecule or molecular complex and not to one or more other molecules or molecular complexes. Other methods that are

provided can be used to identify a compound that binds to at least two molecules or molecular complexes.

=> d bib ab kwic 9

L6 ANSWER 9 OF 10 USPATFULL on STN  
AN 2003:99546 USPATFULL  
TI Multi-target analysis of gene families for chemistry of high affinity and selective small molecules and other therapeutics  
IN Arrowsmith, Cheryl, North York, CANADA  
Greenblatt, Jack, Toronto, CANADA  
Edwards, Aled, Toronto, CANADA  
Mendlein, John D., Encincitas, CA, UNITED STATES  
PI US 2003068651 A1 20030410  
AI US 2002-97194 A1 20020312 (10)  
PRAI US 2001-275216P 20010312 (60)  
DT Utility  
FS APPLICATION  
LREP FOLEY HOAG LLP, PATENT GROUP, WORLD TRADE CENTER WEST, 155 SEAPORT BOULEVARD, BOSTON, MA, 02110-2600  
CLMN Number of Claims: 79  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 5161  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to methods for learning structural information about a molecule or molecular complex. The invention also provides methods for identifying a compound that binds to a molecule or molecular complex. The invention also provides methods for identifying a compound that binds to one molecule or molecular complex and not to one or more other molecules or molecular complexes. Other methods that are provided can be used to identify a compound that binds to at least two molecules or molecular complexes.

SUMM [0049] A " \*\*\*fusion\*\*\* \*\*\*protein\*\*\* " or "fusion polypeptide" refers to a polypeptide comprising a first amino acid sequence encoding a polypeptide linked to at least . . . not substantially homologous with any domain of the first polypeptide. The two polypeptide sequences may be linked in frame. A \*\*\*fusion\*\*\* \*\*\*protein\*\*\* may include a domain which is found (albeit in a different protein) in an organism which also expresses the first. . . . fusion polypeptides may be fused to the N-terminus, the C-terminus, or the N- and C-terminus of the first polypeptide. Exemplary \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* include polypeptides comprising a glutathione S-transferase tag (GST-tag), histidine tag (His-tag), an immunoglobulin domain or an immunoglobulin binding domain.

SUMM . . . synthesizer or by recombinant techniques or combinations thereof), a recombinant test compound, a natural or a non-natural test compound, a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* or equivalent thereof and mutants, derivatives or combinations thereof.

SUMM [0135] In certain embodiments, a polypeptide which may be used in accordance with the methods of the invention is a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* containing a domain which increases its solubility and/or facilitates its purification, identification, detection, and/or structural or functional characterization. Exemplary domains, . . . protein A, protein G, calmodulin-binding peptide, thioredoxin, maltose binding protein, HA, myc, poly arginine, poly His, poly His-Asp or FLAG \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* and tags. Additional exemplary domains include domains that alter protein localization in vivo, such as signal peptides, type III secretion. . . . the invention to include linker sequences between the polypeptide and the fusion domain in order to facilitate construction of the \*\*\*fusion\*\*\* \*\*\*protein\*\*\* or to optimize protein expression or structural constraints of the \*\*\*fusion\*\*\* \*\*\*protein\*\*\*. In another embodiment, the polypeptide may be constructed so as to contain protease cleavage sites between the fusion polypeptide and. . .

SUMM . . . Chem 269:10444-10450; and Perez et al. (1992) J Cell Sci 102:717-722). The transcytosis polypeptide may also be a non-naturally occurring membrane- \*\*\*translocating\*\*\* sequence (MTS), such as the peptide sequences disclosed in U.S. Pat. No. 6,248,558.

SUMM . . . of the invention may be tested for binding activity, as well as

inhibitory ability, by expression as, for example, thioredoxin \*\*\*fusion\*\*\* \*\*\*proteins\*\*\*, each of which contains a discrete fragment of a protein of the invention (see, for example, U.S. Pat. Nos. 5,270,181. . .

SUMM . . . that the degenerate set of potential nucleotide sequences are expressible as individual polypeptides, or alternatively, as a set of larger \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* (e.g. for phage display).

SUMM . . . et al., WO 88/06630; Fuchs et al., (1991) Bio/Technology 9:1370-1371; and Goward et al., (1992) TIBS 18:136-140), and the resulting \*\*\*fusion\*\*\* \*\*\*protein\*\*\* detected by panning, e.g. using a fluorescently labeled molecule which binds the cell surface protein, e.g. FITC-substrate, to score for. . .

SUMM [0157] In similar fashion, the gene library may be expressed as a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* on the surface of a viral particle. For instance, in the filamentous phage system, foreign peptide sequences may be expressed. . . used in phage display libraries, as either of the phage gIII or gVIII coat proteins may be used to generate \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* without disrupting the ultimate packaging of the viral particle (Ladner et al., PCT publication WO 90/02909; Garrard et al., PCT. . .

SUMM . . . construct which includes coding sequences for a late vaccinia virus structural protein to produce a set of recombinant viruses expressing \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* comprising a portion of the protein as part of the virion. The Hepatitis B surface antigen may also be utilized in this role as well. Similarly, chimeric constructs coding for \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* containing a portion of a polypeptide and the poliovirus capsid protein may be created to enhance immunogenicity (see, for example, . . .

SUMM . . . cleavage site sequence at the N-terminus of the desired portion of the recombinant protein, may allow purification of the expressed \*\*\*fusion\*\*\* \*\*\*protein\*\*\* by affinity chromatography using a Ni.sup.2+ metal resin. The purification leader sequence may then be subsequently removed by treatment with. . .

DETD . . . GRK-7 AF282269

receptor kinases

(GRKs)

Hexokinase cancer

type II

NM\_000189

Casein Kinase

Glycogen

Synthase Kinase

(GSK),

LIM Kinase

(actin-binding

kinase

\*\*\*IkappaB\*\*\*

Kinases (IKK),

Rock and Related

Rho Interacting

Proteins (protein

kinases)

Pyruvate

Dehydrogenase

Kinase (PDK)

IL-1 receptor

kinases

Calcium/calmodu

lin-dependent

protein. . .

=> d bib ab kwic 1-8

L6 ANSWER 1 OF 10 USPATFULL on STN

AN 2004:306965 USPATFULL

TI Monitoring gene silencing and annotating gene function in living cells

IN Michnick, Stephen William Watson, Westmount, CANADA

Belisle, Barbara, Moraga, CA, UNITED STATES

MacDonald, Marnie L., Pleasanton, CA, UNITED STATES

Westwick, John K., San Ramon, CA, UNITED STATES

Lamerdin, Jane Elizabeth, Livermore, CA, UNITED STATES

WO3 002598

PI US 2004241636 A1 20041202  
AI US 2004-856620 A1 20040529 (10)  
PRAI US 2003-474283P 20030530 (60)  
DT Utility  
FS APPLICATION  
LREP Isaac A. Angres, Suite 301, 2001 Jefferson Davis Highway, Arlington, VA,  
22202  
CLMN Number of Claims: 14  
ECL Exemplary Claim: 1  
DRWN 16 Drawing Page(s)  
LN.CNT 2073

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The cell-based assays described in the present invention can be used to directly assess the sensitivity and specificity of the gene annotation reagent against its target, and to determine if a non-targeted gene participates in a pathway of interest or is functionally linked to another gene or protein. The combination of annotation reagents with such cell-based assays is useful for mapping genes (proteins) into cellular pathways on a genome-wide scale. Preferred assay embodiments include fluorescence or luminescence assays in intact (live or fixed) cells. Such fluorescence or luminescence assays include high-throughput or high-content assays for protein activity, subcellular localization, post-translational modifications, or interactions of proteins. Suitable assays may include protein-protein interaction assays; protein translocation assays; and post-translational modification assays. The invention can be used to assess the efficacy of any gene silencing experiment, to determine the level of gene silencing that is achieved, and to map novel genes into biochemical pathways, and to identify novel pharmaceutical targets. The results also demonstrate the feasibility of employing this strategy in genome-wide functional annotation efforts.  
DETDX . . . RNAi silencing of AKT would result in failure of BAD to phosphorylate at ser site 136, thus preventing BAD from \*\*\*translocating\*\*\* to the cytosol and forming complexes with 14-3-3sigma. In our experiments, cotransfection of this pair with siAKT resulted in a . . .  
DETDX . . . NFkappaB as a fusion with a luminophore--such as GFP or YFP--and monitoring the redistribution of signal generated by the p65 \*\*\*fusion\*\*\* \*\*\*protein\*\*\* ; or alternatively co-expressing p65 tagged with a fragment of GFP or YFP along with the other (p50) subunit of NFkappa . . .  
DETDX . . . genes for two different fluorescent reporters, capable of undergoing FRET are separately fused to genes encoding of interest, and the \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* are co-expressed in live cells. When a protein complex forms between the proteins of interest, the fluorophores are brought into. . .  
DETDX [0139] Schmid, J. A., et al. (2000) Dynamics of NFkappaB and \*\*\*IkappaBalphalpha\*\*\* studied with green fluorescent protein (GFP)  
\*\*\*fusion\*\*\* \*\*\*proteins\*\*\* . J. Biol. Chem. 275 (22): 17035-17042.

L6 ANSWER 2 OF 10 USPATFULL on STN  
AN 2004:298665 USPATFULL  
TI Peptides for use as translocation factors  
IN Crisanti, Andreia, London, UNITED KINGDOM  
PI US 2004234527 A1 20041125  
AI US 2004-479166 A1 20040429 (10)  
WO 2002-GB3027 20020701  
PRAI GB 2001-16047 20010629  
DT Utility  
FS APPLICATION  
LREP SALIWANCHIK LLOYD & SALIWANCHIK, A PROFESSIONAL ASSOCIATION, PO BOX 142950, GAINESVILLE, FL, 32614-2950  
CLMN Number of Claims: 39  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 1271

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Proteins that contain the amino acid sequence motif X.sup.1X.sup.1X.sup.2X.sup.3X.sup.1, where X.sup.1=R or K and X.sup.2 and X.sup.3=any amino acid have been found to translocate and can therefore be used in the manufacture of compositions for therapeutic applications. The proteins may also be used as translocation factors to

SO School, Nashville, TN, 37232, USA  
Journal of Immunology (2001), 166(4), 2218-2227  
CODEN: JOIMA3; ISSN: 0022-1767  
PB American Association of Immunologists  
DT Journal  
LA English  
AB Proliferative responses of lymphoid cells to IL-2 and IL-4 depend on activation of the cells, but the mechanism(s) by which activation enhances cellular competence to respond to cytokines is not fully understood. The NF-.kappa.B/Rel family represents one signal transduction pathway induced during such activation. We show in this study that inhibition of NF-.kappa.B through the expression of an I.kappa.B.alpha. (inhibitory protein that dissocts from NF-.kappa.B) mutant refractory to signal-induced degrdn. (I.kappa.B.alpha.(.DELTA.N)) interfered with the acquisition of competence to proliferate in response to IL-4 as well as IL-2. Thymocytes and T cells from I.kappa.B.alpha.(.DELTA.N) transgenic mice expressed normal levels of IL-2R subunits. However, transgenic cells exhibited a dramatic defect in Stat5A activation treatment with IL-2, and a similar defect was obsd. for IL-4-induced Stat5. In contrast, T lymphoid cells with inhibition of NF-.kappa.B showed normal insulin receptor substrate-2 phosphorylation and only a modest decrease in Stat6 activation and insulin receptor substrate-1 phosphorylation after IL-4 stimulation. These results indicate that the NF-.kappa.B/Rel/I.kappa.B.alpha. system can regulate cytokine receptor capacitation through effects on the induction of downstream signaling by the Stat transcription factor family.

RE.CNT 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2001:906547 CAPLUS  
DN 136:149534  
TI NF-.kappa.B activation plays an important role in the IL-4-induced protection from apoptosis  
AU Zamorano, Jose; \*\*\*Mora, Ana L.\*\*\* ; Boothby, Mark; Keegan, Achsah D.  
CS Department of Immunology, Holland Laboratory, American Red Cross,  
Rockville, MD, 20855, USA  
SO International Immunology (2001), 13(12), 1479-1487  
CODEN: INIMEN; ISSN: 0953-8178  
PB Oxford University Press  
DT Journal  
LA English  
AB IL-4 alone protects cells from apoptosis by insulin receptor substrate (IRS)-dependent and -independent mechanisms. However, *in vivo* cells are typically exposed to a no. of signals at the same time. To det. the contribution of co-stimulatory signals to the regulation of apoptosis by IL-4, the authors first analyzed whether tumor necrosis factor (TNF)-.alpha., which has been shown to inhibit the activation of IRS-1 by insulin, could modify IL-4 signaling and protection from apoptosis. The authors found that TNF-.alpha. cooperates with IL-4 in protecting 32D cells from factor withdrawal-induced apoptosis. This effect was independent of the expression of IRS-1, indicating that this cooperation is via an alternative anti-apoptotic pathway. Moreover, TNF-.alpha. had no effect on the activation of IRS-1 induced by IL-4. IL-4 enhanced TNF-.alpha.-induced activation of the transcription factor NF-.kappa.B. Interestingly, pharmacol. inhibition of NF-.kappa.B activation or protein synthesis resulted in the induction of cell death that could not be inhibited by IL-4, suggesting that IL-4 cooperates with NF-.kappa.B to signal protection from apoptosis. Supporting this hypothesis, IL-4 also increased NF-.kappa.B activation induced by anti-CD3 antibodies in primary T cells and protected them from apoptosis induced by receptor engagement. However, IL-4 was not able to inhibit apoptosis induced by anti-CD3 in T lymphocytes isolated from transgenic mice expressing a dominant-neg. form of I.kappa.B.alpha. that prevents NF-.kappa.B activation. Thus, in addn. to the previously identified IRS-1 pathway, IL-4-induced protection from apoptosis may also be mediated through cooperation with the NF-.kappa.B family of transcription factors.

RE.CNT 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN

deliver proteins or nucleic acids into a cell.

SUMM . . . comprises the amino acid sequence defined above. The agent is therefore able to gain entry into the cell using the \*\*\*translocating\*\*\* properties of the peptide.

SUMM [0012] According to a further aspect of the present invention, there is a conjugate of a peptide capable of \*\*\*translocating\*\*\* across a cell membrane, and a therapeutic, diagnostic or cosmetic agent, wherein the peptide comprises the amino acid sequence motif. . . .

SUMM [0014] In contrast to conventional \*\*\*translocating\*\*\* agents such as tat, VP22 or antennapedia, the present invention permits human-derived peptides to be used as the translocation factor,. . . .

SUMM . . . of the invention, an expression vector is prepared that expresses a conjugate of the invention in the form of a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* .

DETD [0019] Identifying this sequence enables many different \*\*\*translocating\*\*\* peptides to be produced.

DETD [0022] The \*\*\*translocating\*\*\* peptide may be in a truncated form or in a synthetic form, which can be produced readily, without the need. . . .

DETD [0023] In a preferred embodiment, the \*\*\*translocating\*\*\* peptide fragment comprises no more than 50, preferably no more than 40, and most preferably no more than 30 amino. . . .

DETD [0029] Functional variants of the \*\*\*translocating\*\*\* peptides/proteins may also be used. For example, proteins with high levels (greater than 70%, preferably greater than 90% and more. . . .

DETD [0033] Compositions containing the protein to be administered may comprise any suitable excipient, diluent or buffer. No other \*\*\*translocating\*\*\* factor is required.

DETD [0043] The present invention also enables peptides comprising the motif to be used as the \*\*\*translocating\*\*\* vehicle for the delivery of other therapeutic, diagnostic or cosmetic agents across a cell membrane to effect entry of the. . . .

DETD [0044] Peptides having the motif may therefore be used to prepare conjugates having the \*\*\*translocating\*\*\* region and a heterologous therapeutic agent.

DETD [0045] The term "conjugate" refers to a chimeric molecule formed from a \*\*\*translocating\*\*\* peptide and a therapeutic, diagnostic or cosmetic agent.

DETD . . . may be in the form of a chemical linker molecule, or the product may be in the form of a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* .

DETD [0048] The \*\*\*translocating\*\*\* peptides may comprise the defined sequence motif more than once, for example two or three motifs may be present.

DETD [0049] The \*\*\*translocating\*\*\* peptides may also comprise a high percentage of Lys and Arg residues, typically greater than 5%, preferably more than 10%. . . .

DETD [0050] In addition to the \*\*\*translocating\*\*\* peptides identified herein, the conjugates comprise a discrete, i.e. heterologous, therapeutic, diagnostic or cosmetic agent. In the context of the. . . .

DETD . . . linked via a covalent attachment. In one embodiment the agent is a peptide (or protein) and the conjugate is a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* . The production of \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* is known to those skilled in the art and comprises the production of a recombinant polynucleotide that encodes, in frame,. . . .

DETD [0064] The proteins, whether to be administered as a replacement therapy, or for use as a \*\*\*translocating\*\*\* peptide, may also be modified to include additional substituents that help to target the protein/peptide to a particular cell. For. . . .

DETD . . . (Somatomedin C). Acc.

No. P05019

9. Inhibitor of nuclear factor kappa-B kinase alpha subunit (I kappa-B kinase alpha) (IkBKA) (IKK-alpha) (IKK-A) ( \*\*\*IkappaB\*\*\* kinase) (I-kappa-B kinase 1) (IKK1)  
(Conserved helix-loop-helix ubiquitous kinase) (Nuclear factor NFkappaB inhibitor kinase alpha) (NFKBIKA). Acc. No. O15111

10. Interferon. . . .

DETD . . . of translocation was carried out by reading the activity of a beta.-Galactosidase enzyme that was included as part of a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* with the translocation agents. When provided with the appropriate galactoside substrate, the enzyme deglycosylates the substrate leading to the accumulation. . . .

provided a sensitive means of detecting the amount of the .beta.-Galactosidase present in the samples, and ultimately, the amount of \*\*\*fusion\*\*\* \*\*\*protein\*\*\* delivered into the cells..

CLM What is claimed is:

27. The conjugate according to claim 14, which is a \*\*\*fusion\*\*\* \*\*\*protein\*\*\*.

31. An expression vector that encodes a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* wherein said \*\*\*fusion\*\*\* \*\*\*protein\*\*\* is a conjugate of a peptide capable of translocation across a cell membrane, and a therapeutic or diagnostic agent, wherein.

32. A recombinant cell line comprising an expression vector that encodes a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* wherein said \*\*\*fusion\*\*\* \*\*\*protein\*\*\* is a conjugate of a peptide capable of translocation across a cell membrane, and a therapeutic or diagnostic agent, wherein.

L6 ANSWER 3 OF 10 USPATFULL on STN  
AN 2004:196424 USPATFULL  
TI Lectin compositions and methods for modulating an immune response to an antigen  
IN Segal, Andrew H., Boston, MA, UNITED STATES  
Young, Elihu, Sharon, MA, UNITED STATES  
PA Genitrix, LLC (U.S. corporation)  
PI US 2004151728 A1 20040805  
AI US 2003-666834 A1 20030919 (10)  
RLI Division of Ser. No. US 2003-645000, filed on 20 Aug 2003, PENDING  
PRAI US 2002-404823B 20020820 (60)  
US 2003-487407P 20030715 (60)  
DT Utility  
FS APPLICATION  
LREP PALMER & DODGE, LLP, KATHLEEN M. WILLIAMS, 111 HUNTINGTON AVENUE,  
BOSTON, MA, 02199  
CLMN Number of Claims: 77  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 39129

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a fusion polypeptide which can bind to a cell surface binding moiety (e.g., a carbohydrate) and serve as a ligand for a cell surface polypeptide, as well as a vector comprising a nucleic acid encoding for such a fusion polypeptide, and a host cell comprising such nucleic acid. The present invention also provides a composition comprising an antigen bearing target and such a fusion polypeptide, as well as a composition comprising a virus or a cell and such a fusion polypeptide. The present invention further relates to a method of modulating an immune response in an animal using such compositions.

SUMM . . . an animal comprising administering to said animal a composition comprising a cell comprising an antigen, said composition further comprising a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* comprising a lectin and a ligand for a cell surface protein.

SUMM . . . an animal comprising administering to said animal a composition comprising a cell comprising an antigen, said composition further comprising a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* comprising a lectin and a ligand for a cell surface protein.

DETD DETAILED DESCRIPTION

[0097] The present invention is based, in part, on the discovery that a multifunctional \*\*\*fusion\*\*\* \*\*\*protein\*\*\* comprising a first polypeptide which is a lectin and a second polypeptide which is a ligand of a cell surface. . .

DETD [0196] A stable and highly bioactive designer cytokine consisting of a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* between IL6 and a soluble IL6 receptor, designated H-IL6, has been used for human hematopoietic progenitor cell expansion and is. . .

DETD [0225] Bioactive murine and human IL12 \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* combining the two IL12 subunits in a single molecule have been described. This designer cytokine retains antitumor activity in vivo..

DETD . . . viral antigens such as hemagglutinin and neuraminidase and other influenza viral components; measles viral antigens such as the

measles virus \*\*\*fusion\*\*\* \*\*\*protein\*\*\* and other measles virus components; rubella viral antigens such as proteins E1 and E2 and other rubella virus components; rotaviral. . . cytomegaloviral antigens such as envelope glycoprotein B and other cytomegaloviral antigen components; respiratory syncytial viral antigens such as the RSV \*\*\*fusion\*\*\* \*\*\*protein\*\*\*, the M2 protein and other respiratory syncytial viral antigen components; herpes simplex viral antigens such as immediate early proteins, glycoprotein. . .

DETD . . . to the manufacturer's instructions. The purified HA1 DNA fragment was digested with Nhe I and Kpn I. To make the \*\*\*fusion\*\*\* \*\*\*protein\*\*\*, the purified Nhe 1-Kpn I HA fragment was ligated into the pUC 19 GM-CSF-K-Gas1.1 vector that had been digested with. . .

DETD [5836] Homo sapiens LDLR-FUT \*\*\*fusion\*\*\* \*\*\*protein\*\*\* (LDLR-FUT) mRNA, complete cds

DETD [5968] Homo sapiens partial mRNA for BCR/FGFR1 chimaeric \*\*\*fusion\*\*\* \*\*\*protein\*\*\*

DETD [7849] Homo sapiens translocation associated \*\*\*fusion\*\*\* \*\*\*protein\*\*\* IRTA1/IGA1 (IRTA1/IGHA1) mRNA, complete cds

DETD [11789] Homo sapiens tumor necrosis factor receptor superfamily, member 12 ( \*\*\*translocating\*\*\* chain-association membrane protein) (TNFRSF12), mRNA

DETD [14874] Homo sapiens neurotrophic receptor tyrosine kinase-ETS related protein \*\*\*fusion\*\*\* \*\*\*protein\*\*\* (NTRK3-ETV6 fusion) mRNA, partial cds

DETD [14877] Homo sapiens ETS related protein-neurotrophic receptor tyrosine kinase \*\*\*fusion\*\*\* \*\*\*protein\*\*\* (ETV6-NTRK3 fusion) mRNA, partial cds

DETD [16811] 11503: AF101784

[16812] Homo sapiens b-TRCP variant E3RS- \*\*\*IkappaB\*\*\* mRNA, partial cds

L6 ANSWER 4 OF 10 USPATFULL on STN  
AN 2004:165307 USPATFULL  
TI Lectin compositions and methods for modulating an immune response to an antigen  
IN Segal, Andrew H., Boston, MA, UNITED STATES  
Young, Elihu, Sharon, MA, UNITED STATES  
PA Genitrix, LLC (U.S. corporation)  
PI US 2004126793 A1 20040701  
AI US 2003-666885 A1 20030919 (10)  
RLI Division of Ser. No. US 2003-645000, filed on 20 Aug 2003, PENDING  
PRAI US 2002-404823P 20020820 (60)  
US 2003-487407P 20030715 (60)  
DT Utility  
FS APPLICATION  
LREP PALMER & DODGE, LLP, KATHLEEN M. WILLIAMS, 111 HUNTINGTON AVENUE, BOSTON, MA, 02199  
CLMN Number of Claims: 147  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 28979  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB The present invention provides a fusion polypeptide which can bind to a cell surface binding moiety (e.g., a carbohydrate) and serve as a ligand for a cell surface polypeptide, as well as a vector comprising a nucleic acid encoding for such a fusion polypeptide, and a host cell comprising such nucleic acid. The present invention also provides a composition comprising an antigen bearing target and such a fusion polypeptide, as well as a composition comprising a virus or a cell and such a fusion polypeptide. The present invention further relates to a method of modulating an immune response in an animal using such compositions.  
SUMM . . . an animal comprising administering to said animal a composition comprising a cell comprising an antigen, said composition further comprising a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* comprising a lectin and a ligand for a cell surface protein.  
SUMM . . . an animal comprising administering to said animal a composition comprising a cell comprising an antigen, said composition further comprising a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* comprising a lectin and a ligand for a cell surface protein.  
SUMM [0097] The present invention is based, in part, on the discovery that a

multifunctional \*\*\*fusion\*\*\* \*\*\*protein\*\*\* comprising a first polypeptide which is a lectin and a second polypeptide which is a ligand of a cell surface. . .

SUMM [0196] A stable and highly bioactive designer cytokine consisting of a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* between IL6 and a soluble IL6 receptor, designated H-IL6, has been used for human hematopoietic progenitor cell expansion and is. . .

SUMM [0225] Bioactive murine and human IL12 \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* combining the two IL12 subunits in a single molecule have been described. This designer cytokine retains antitumor activity in vivo.. . .

SUMM . . . viral antigens such as hemagglutinin and neuraminidase and other influenza viral components; measles viral antigens such as the measles virus \*\*\*fusion\*\*\* \*\*\*protein\*\*\*, and other measles virus components; rubella viral antigens such as proteins E1 and E2 and other rubella virus components; rotaviral. . . cytomegaloviral antigens such as envelope glycoprotein B and other cytomegaloviral antigen components; respiratory syncytial viral antigens such as the RSV \*\*\*fusion\*\*\* \*\*\*protein\*\*\*, the M2 protein and other respiratory syncytial viral antigen components; herpes simplex viral antigens such as immediate early proteins, glycoprotein. . .

DETD . . . to the manufacturer's instructions. The purified HA1 DNA fragment was digested with Nhe I and Kpn I. To make the \*\*\*fusion\*\*\* \*\*\*protein\*\*\*, the purified Nhe I-Kpn I HA fragment was ligated into the pUC19 GM-CSF-K-Gas1.1 vector that had been digested with Nhe. . .

DETD [2485] 2404: AF117899 Homo sapiens LDLR-FUT \*\*\*fusion\*\*\* \*\*\*protein\*\*\* (LDLR-FUT) mRNA, complete cds gi|6739499|gb|AF117899.1|AF117899[6739499]

DETD [2527] 2457: AJ298916 Homo sapiens partial mRNA for BCR/FGFR1 chimaeric \*\*\*fusion\*\*\* \*\*\*protein\*\*\* gi|16444911|emb|AJ298916.1|HSA298916[16444911]

DETD [3126] 4842: AF343666 Homo sapiens translocation associated \*\*\*fusion\*\*\* \*\*\*protein\*\*\* IRTA1/IGA1 (IRTA1/IGHA1) mRNA, complete cds gi|13591717|gb|AF343666.1|AF343666[13591717]

DETD [4398] 6991: NM.sub.--003790 Homo sapiens tumor necrosis factor receptor superfamily, member 12 ( \*\*\*translocating\*\*\* chain-association membrane protein) (TNFRSF12), mRNA gi|4507568|ref|NM.sub.--003790.1|[4507568]

DETD [5031] 8873: AF041811 Homo sapiens ETS related protein-growth factor receptor tyrosine kinase \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* (ETV6-NTRK3 fusion) mRNA, partial cds gi|6274523|gb|AF041811.2|AF041811[6274523]

DETD [5407] 9538: AF125809 Homo sapiens neurotrophic receptor tyrosine kinase-ETS related protein \*\*\*fusion\*\*\* \*\*\*protein\*\*\* (NTRK3-ETV6 fusion) mRNA, partial cds gi|6635288|gb|AF125809.1|AF125809[6635288]

DETD [5408] 9539: AF125808 Homo sapiens ETS related protein-neurotrophic receptor tyrosine kinase \*\*\*fusion\*\*\* \*\*\*protein\*\*\* (ETV6-NTRK3 fusion) mRNA, partial cds gi|6635286|gb|AF125808.1|AF125808[6635286]

DETD [6035] 11503: AF101784 Homo sapiens b-TRCP variant E3RS- \*\*\*IkappaB\*\*\* mRNA, partial cds gi|4165135|gb|AF101784.1|AF101784[4165135]

L6 ANSWER 5 OF 10 USPATFULL on STN  
AN 2004:164872 USPATFULL  
TI Lectin compositions and methods for modulating an immune response to an antigen  
IN Segal, Andrew H., Boston, MA, UNITED STATES  
Young, Elihu, Sharon, MA, UNITED STATES  
PA Genitrix, LLC (U.S. corporation)  
PI US 2004126357 A1 20040701  
AI US 2003-666886 A1 20030919 (10)  
RLI Division of Ser. No. US 2003-645000, filed on 20 Aug 2003, PENDING  
PRAI US 2002-404823P 20020820 (60)  
US 2003-487407P 20030715 (60)  
DT Utility  
FS APPLICATION  
LREP PALMER & DODGE, LLP, KATHLEEN M. WILLIAMS, 111 HUNTINGTON AVENUE,  
BOSTON, MA, 02199  
CLMN Number of Claims: 11  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 39007

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a fusion polypeptide which can bind to a cell surface binding moiety (e.g., a carbohydrate) and serve as a ligand for a cell surface polypeptide, as well as a vector comprising a nucleic acid encoding for such a fusion polypeptide, and a host cell comprising such nucleic acid. The present invention also provides a composition comprising an antigen bearing target and such a fusion polypeptide, as well as a composition comprising a virus or a cell and such a fusion polypeptide. The present invention further relates to a method of modulating an immune response in an animal using such compositions.

SUMM . . . an animal comprising administering to said animal a composition comprising a cell comprising an antigen, said composition further comprising a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* comprising a lectin and a ligand for a cell surface protein.

SUMM . . . an animal comprising administering to said animal a composition comprising a cell comprising an antigen, said composition further comprising a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* comprising a lectin and a ligand for a cell surface protein.

DETD DETAILED DESCRIPTION

[0097] The present invention is based, in part, on the discovery that a multifunctional \*\*\*fusion\*\*\* \*\*\*protein\*\*\* comprising a first polypeptide which is a lectin and a second polypeptide which is a ligand of a cell surface. . .

DETD [0196] A stable and highly bioactive designer cytokine consisting of a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* between IL6 and a soluble IL6 receptor, designated H-IL6, has been used for human hematopoietic progenitor cell expansion and is. . .

DETD [0225] Bioactive murine and human IL12 \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* combining the two IL12 subunits in a single molecule have been described. This designer cytokine retains antitumor activity in vivo..

DETD . . . viral antigens such as hemagglutinin and neuraminidase and other influenza viral components; measles viral antigens such as the measles virus \*\*\*fusion\*\*\* \*\*\*protein\*\*\* and other measles virus components; rubella viral antigens such as proteins E1 and E2 and other rubella virus components; rotaviral. . . . cytomegaloviral antigens such as envelope glycoprotein B and other cytomegaloviral antigen components; respiratory syncytial viral antigens such as the RSV \*\*\*fusion\*\*\* \*\*\*protein\*\*\*, the M2 protein and other respiratory syncytial viral antigen components; herpes simplex viral antigens such as immediate early proteins, glycoprotein. . .

DETD . . . to the manufacturer's instructions. The purified HA1 DNA fragment was digested with Nhe I and Kpn I. To make the \*\*\*fusion\*\*\* \*\*\*protein\*\*\*, the purified Nhe 1-Kpn I HA fragment was ligated into the pUC 19 GM-CSF-K-Gas1.1 vector that had been digested with. . .

DETD [5805] Homo sapiens LDLR-FUT \*\*\*fusion\*\*\* \*\*\*protein\*\*\* (LDLR-FUT) mRNA, complete cds

DETD [5937] Homo sapiens partial mRNA for BCR/FGFR1 chimaeric \*\*\*fusion\*\*\* \*\*\*protein\*\*\*

DETD [7818] Homo sapiens translocation associated \*\*\*fusion\*\*\* \*\*\*protein\*\*\* IRTA1/IGA1 (IRTA1/IGHA1) mRNA, complete cds

DETD [11758] Homo sapiens tumor necrosis factor receptor superfamily, member 12 ( \*\*\*translocating\*\*\* chain-association membrane protein) (TNFRSF12), mRNA

DETD [14843] Homo sapiens neurotrophic receptor tyrosine kinase-ETS related protein \*\*\*fusion\*\*\* \*\*\*protein\*\*\* (NTRK3-ETV6 fusion) mRNA, partial cds

DETD [14846] Homo sapiens ETS related protein-neurotrophic receptor tyrosine kinase \*\*\*fusion\*\*\* \*\*\*protein\*\*\* (ETV6-NTRK3 fusion) mRNA, partial cds

DETD [16780] 11503: AF101784

[16781] Homo sapiens b-TRCP variant E3RS- \*\*\*IkappaB\*\*\* mRNA, partial cds

L6 ANSWER 6 OF 10 USPATFULL on STN

AN 2004:12959 USPATFULL

TI Methods and compositions for diagnosing or monitoring auto immune and chronic inflammatory diseases

IN Wohlgemuth, Jay, Palo Alto, CA, UNITED STATES

Fry, Kirk, Palo Alto, CA, UNITED STATES  
 Woodward, Robert, Pleasanton, CA, UNITED STATES  
 Ly, Ngoc, San Bruno, CA, UNITED STATES  
 PI US 2004009479 A1 20040115  
 AI US 2002-131827 A1 20020424 (10)  
 RLI Continuation-in-part of Ser. No. US 2001-6290, filed on 22 Oct 2001,  
 PENDING  
 PRAI US 2001-296764P 20010608 (60)  
 DT Utility  
 FS APPLICATION  
 LREP Michael R. Ward, Morrison & Foerster LLP, 425 Market Street, San  
 Francisco, CA, 94105-2482  
 CLMN Number of Claims: 19  
 ECL Exemplary Claim: 1  
 DRWN 12 Drawing Page(s)  
 LN.CNT 19677  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB Methods of diagnosing or monitoring an autoimmune or chronic  
 inflammatory disease, particularly SLE in a patient by detecting the  
 expression level of one or more genes or surrogates derived therefrom in  
 the patient are described. Diagnostic oligonucleotides for diagnosing or  
 monitoring chronic inflammatory disease, particularly SLE infection and  
 kits or systems containing the same are also described.  
 DETD . . . to produce the protein encoded by the novel nucleotide sequence  
 for such assay systems, it may be advantageous to engineer  
 \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* that can facilitate labeling,  
 immobilization and/or detection.  
 DETD . . . Hs.129780 SWAP70  
 Hs.153026  
 TNFRSF10d Hs.129844 DOM-3 (C. elegans)  
 homolog Z Hs.153299  
 POLL Hs.129903  
 Hs.153551  
 GADD153 = growth arrest and DNA-damage Hs.129913  
 Hs.15370  
 inducible gene/fus-chop \*\*\*fusion\*\*\* \*\*\*protein\*\*\*  
 solute carrier family 5 (neutral amino acid Hs.130101 SMAD6  
 Hs.153863  
 transporters, system A), member 4  
 Hs.130232 APEXL2  
 Hs.154149 Hs.13034  
 Hs.154198  
 CD30L Hs.1313  
 Hs.154366  
 SCYA26. . .  
 DETD . . . 1130 1630 X52882 Hs.4112 0 6  
 polypeptide 1 gene/cds = (21,1691)/  
 gb = X528  
 176A7 515 892 BC000687 Hs.4147 0 1  
 \*\*\*translocating\*\*\* chain-associating membrane p  
 185B5 3480 3707 AB023216 Hs.4278 1.00E-86 1  
 mRNA for KIAA0999 protein, partial cds/cds = (0  
 154E12 1731 2531 AF079566. . .  
 DETD . . . = (53,2296)/gb =  
 122E5 1060 1294 NM\_002893 Hs.31314 1.00E-113 1  
 retinoblastoma-binding protein 7 (RBBP7), mR  
 117B1 2056 2489 AF153419 Hs.31323 0 1  
 \*\*\*IkappaBkinase\*\*\* complex-associated protein (I  
 462E10 337 569 AV752358 Hs.31409 1.00E-108 1  
 AV752358 cDNA, 5' end/clone = NPDBHG03/clone.sub.--  
 126E7 1962 2748 AB014548 Hs.31921 0. . .  
 DETD . . . 324 682 BE540238 Hs.180549 1.00E-143 1  
 601059809F1 cDNA, 5' end/clone = IMAGE: 3446283  
 68G8 1447 3594 AF123094 Hs.180566 0 3  
 API2-MLT \*\*\*fusion\*\*\* \*\*\*protein\*\*\* (API2-MLT) mRNA, comp  
 180B9 1851 2142 NM\_002087 Hs.180577 1.00E-160 2  
 granulin (GRN), mRNA/cds = (62,1843)/gb = NM\_00  
 51E4 880 2466 NM\_005066 Hs.180610. . .

AN 2003:220740 USPATFULL  
TI Methods and compositions for diagnosing and treating rheumatoid arthritis  
IN Pittman, Debra D., Windham, NH, UNITED STATES  
Feldman, Jeffrey L., Arlington, MA, UNITED STATES  
Shields, Kathleen M., Harvard, MA, UNITED STATES  
Trepicchio, William L., Andover, MA, UNITED STATES  
PI US 2003154032 A1 20030814  
AI US 2001-23451 A1 20011217 (10)  
PRAI US 2000-255861P 20001215 (60)  
DT Utility  
FS APPLICATION  
LREP Patent Group, FOLEY, HOAG & ELIOT LLP, One Post Office Square, Boston, MA, 02109  
CLMN Number of Claims: 40  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 25385

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides methods and compositions for diagnostic assays for detecting R.A. and therapeutic methods and compositions for treating R.A. The invention also provides methods for designing, identifying, and optimizing therapeutics for R.A. Diagnostic compositions of the invention include compositions comprising detection agents for detecting one or more genes that have been shown to be up- or down-regulated in cells of R.A. relative to normal counterpart cells. Exemplary detection agents include nucleic acid probes, which can be in solution or attached to a solid surface, e.g., in the form of a microarray. The invention also provides computer-readable media comprising values of levels of expression of one or more genes that are up- or down-regulated in R.A.  
SUMM . . . a protein or other variety (e.g. lactose to convert the env protein to an asialoglycoprotein), as well as by generating \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* (e.g. single-chain antibody/env \*\*\*fusion\*\*\* \*\*\*proteins\*\*\*). This technique, while useful to limit or otherwise direct the infection to certain tissue types, and can also be used.  
SUMM . . . any vessel suitable for containing the reactants. Examples include microtitre plates, test tubes, and micro-centrifuge tubes. In one embodiment, a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* can be provided which adds a domain that allows the protein to be bound to a matrix. For example, glutathione-S-transferase/polypeptide (GST/polypeptide) \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* can be adsorbed onto glutathione sepharose beads (Sigma Chemical, St. Louis, Mo.) or glutathione derivatized microtitre plates, which are then. . .  
SUMM . . . intrinsic or extrinsic activity. In the instance of the latter, the enzyme can be chemically conjugated or provided as a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* with the binding partner. To illustrate, the binding partner can be chemically cross-linked or genetically fused with horseradish peroxidase, and. . . in the complex can be assessed with a chromogenic substrate of the enzyme, e.g. 3,3'-diamino-benzidine terahydrochloride or 4-chloro-1-naphthol. Likewise, a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* comprising the polypeptide and glutathione-S-transferase can be provided, and complex formation quantitated by detecting the GST activity using 1-chloro-2,4-dinitrobenzene (Habig. . .  
SUMM . . . be used. Alternatively, the protein to be detected in the complex can be "epitope tagged" in the form of a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* which includes, in addition to the polypeptide sequence, a second polypeptide for which antibodies are readily available (e.g. from commercial sources). For instance, the GST \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* described above can also be used for quantification of binding using antibodies against the GST moiety. Other useful epitope tags. . .

DETD . . . protein S2 ribosomal protein S2  
UBA52\_rnal X56997\_rnal X56997 PASS 9 268.44 PASS  
13 9 198.08 1.36 1.36 UbA52  
ubiquitin-52 amino acid

\*\*\*fusion\*\*\* \*\*\*protein\*\*\*  
RPS18 X69150\_at X69150 PASS 9 377.78 PASS  
13 9 278.77 1.36 1.36 PRS18 6p21.3  
ribosomal protein S18

FCER2	M15059_at	M15059	PASS	9.	.	.	
DETD	.	KIAA0151	D63485	6	Pass	14.33	1 63
13	Pass	TRUE	FALSE		FALSE	6.69	2.14
	IKK-related kinase		1		Kinase		
epsilon, inducible ***IkappaB***							
kinase, IKKE							
39044_s_at	DGKD	D73409	6	Pass	31.67	7 76	
13	Pass	TRUE	FALSE		FALSE	14 77	2.14
diacylglycerol kinase, delta.							
DETD	.	11 50	4 18	13	Pass	TRUE	FALSE
	FALSE	5.15	2.23	tumor necrosis factor			1p36 2
receptor superfamily,							
member 12 ( ***translocating***							
chain-association							
membrane protein):							
38432_at	ISG15	AA203213	6	Pass	16 50	13.82	
10	Pass	TRUE	FALSE		7.40	2.23	
interferon-stimulated 1							
protein,..							

L6 ANSWER 8 OF 10 USPATFULL on STN  
 AN 2003:99724 USPATFULL  
 TI Proteins and druggable regions of proteins  
 IN Edwards, Aled, Toronto, CANADA  
 Arrowsmith, Cheryl, North York, CANADA  
 Greenblatt, Jack, Toronto, CANADA  
 Mendlein, John D., Encinitas, CA, UNITED STATES  
 PI US 2003068831 A1 20030410  
 AI US 2002-97125 A1 20020312 (10)  
 PRAI US 2001-275216P 20010312 (60)  
 DT Utility  
 FS APPLICATION  
 LREP FOLEY HOAG LLP, PATENT GROUP, WORLD TRADE CENTER WEST, 155 SEAPORT  
 BOULEVARD, BOSTON, MA, 02110-2600  
 CLMN Number of Claims: 31  
 ECL Exemplary Claim: 1  
 DRWN No Drawings  
 LN.CNT 4944

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to methods for learning structural information about a molecule or molecular complex. The invention also provides methods for identifying a compound that binds to a molecule or molecular complex. The invention also provides methods for identifying a compound that binds to one molecule or molecular complex and not to one or more other molecules or molecular complexes. Other methods that are provided can be used to identify a compound that binds to at least two molecules or molecular complexes.

SUMM [0049] A " \*\*\*fusion\*\*\* \*\*\*protein\*\*\* " or "fusion polypeptide" refers to a polypeptide comprising a first amino acid sequence encoding a polypeptide linked to at least. . . not substantially homologous with any domain of the first polypeptide. The two polypeptide sequences may be linked in frame. A " \*\*\*fusion\*\*\* \*\*\*protein\*\*\* " may include a domain which is found (albeit in a different protein) in an organism which also expresses the first. . . fusion polypeptides may be fused to the N-terminus, the C-terminus, or the N- and C-terminus of the first polypeptide. Exemplary " \*\*\*fusion\*\*\* \*\*\*protein\*\*\* " include polypeptides comprising a glutathione S-transferase tag (GST-tag), histidine tag (His-tag), an immunoglobulin domain or an immunoglobulin binding domain.

SUMM . . . synthesizer or by recombinant techniques or combinations thereof, a recombinant test compound, a natural or a non-natural test compound, a " \*\*\*fusion\*\*\* \*\*\*protein\*\*\* " or equivalent thereof and mutants, derivatives or combinations thereof.

SUMM [0135] In certain embodiments, a polypeptide which may be used in

accordance with the methods of the invention is a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* containing a domain which increases its solubility and/or facilitates its purification, identification, detection, and/or structural or functional characterization. Exemplary domains, . . . protein A, protein G, calmodulin-binding peptide, thioredoxin, maltose binding protein, HA, myc, poly arginine, poly His, poly His-Asp or FLAG \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* and tags. Additional exemplary domains include domains that alter protein localization in vivo, such as signal peptides, type III secretion. . . . the invention to include linker sequences between the polypeptide and the fusion domain in order to facilitate construction of the \*\*\*fusion\*\*\* \*\*\*protein\*\*\* or to optimize protein expression or structural constraints of the \*\*\*fusion\*\*\* \*\*\*protein\*\*\*. In another embodiment, the polypeptide may be constructed so as to contain protease cleavage sites between the fusion polypeptide and. . .

SUMM . . . Chem 269:10444-10450; and Perez et al. (1992) J Cell Sci 102:717-722). The transcytosis polypeptide may also be a non-naturally occurring membrane- \*\*\*translocating\*\*\* sequence (MTS), such as the peptide sequences disclosed in U.S. Pat. No. 6,248,558.

SUMM . . . of the invention may be tested for binding activity, as well as inhibitory ability, by expression as, for example, thioredoxin \*\*\*fusion\*\*\* \*\*\*proteins\*\*\*, each of which contains a discrete fragment of a protein of the invention (see, for example, U.S. Pat. Nos. 5,270,181. . .

SUMM . . . that the degenerate set of potential nucleotide sequences are expressible as individual polypeptides, or alternatively, as a set of larger \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* (e.g. for phage display).

SUMM . . . et al., WO 88/06630; Fuchs et al., (1991) Bio/Technology 9:1370-1371; and Goward et al., (1992) TIBS 18:136-140), and the resulting \*\*\*fusion\*\*\* \*\*\*protein\*\*\* detected by panning, e.g. using a fluorescently labeled molecule which binds the cell surface protein, e.g. FITC-substrate, to score for. . .

SUMM [0157] In similar fashion, the gene library may be expressed as a \*\*\*fusion\*\*\* \*\*\*protein\*\*\* on the surface of a viral particle. For instance, in the filamentous phage system, foreign peptide sequences may be expressed. . . used in phage display libraries, as either of the phage gIII or gVIII coat proteins may be used to generate \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* without disrupting the ultimate packaging of the viral particle (Ladner et al., PCT publication WO 90/02909; Garrard et al., PCT. . .

SUMM . . . construct which includes coding sequences for a late vaccinia virus structural protein to produce a set of recombinant viruses expressing \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* comprising a portion of the protein as part of the virion. The Hepatitis B surface antigen may also be utilized in this role as well. Similarly, chimeric constructs coding for \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* containing a portion of a polypeptide and the poliovirus capsid protein may be created to enhance immunogenicity (see, for example,. . .

SUMM . . . cleavage site sequence at the N-terminus of the desired portion of the recombinant protein, may allow purification of the expressed \*\*\*fusion\*\*\* \*\*\*protein\*\*\* by affinity chromatography using a Ni.sup.2+ metal resin. The purification leader sequence may then be subsequently removed by treatment with. . .

DETD . . . GRK-7 AF282269

receptor kinases  
(GRKs)

Hexokinase cancer

type II

NM\_000189

Casein Kinase  
Glycogen  
Synthase Kinase  
(GSK),  
LIM Kinase  
(actin-binding  
kinase

\*\*\*IkappaB\*\*\*  
Kinases (IKK),  
Rock and Related  
Rho Interacting  
Proteins (protein  
kinases)

Pyruvate  
Dehydrogenase  
Kinase (PDK)  
IL-1 receptor  
kinases  
Calcium/calmodu  
lin-dependent  
protein. . .

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